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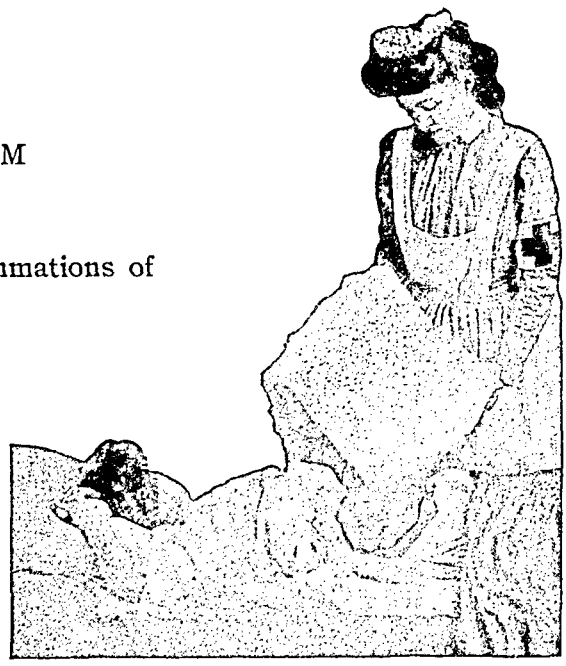

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THE

AMERICAN JOURNAL OF THE MEDICAL SCIENCES.

SEPTEMBER, 1906.

SPECIAL ARTICLES.

I.

TOXEMIC VOMITING OF PREGNANCY.

By J. Whitridge Williams, M.D.,
PROFESSOR OF OBSTETRICS, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND

At the 1905 meeting of the American Gynecological Society I presented in abstract my views concerning the pernicious vomiting of pregnancy, and elaborated them in the *Bulletin of the Johns Hopkins Hospital*, March, 1906. Upon each occasion I stated that the evidence at present available seems to justify one in classifying the serious cases as reflex, neurotic, or toxemic, according to the etiological factors concerned.

In this article, I desire to consider toxemic vomiting more particularly; but before doing so I shall give, as briefly as possible, my reasons for recognizing each of the three varieties, and refer those who are interested in details to my monograph, in which the literature of the subject is exhaustively considered.

In the reflex variety the vomiting is apparently directly attributable to the existence of some abnormality of the generative tract, such as a retroflexion of the uterus or an ovarian tumor, and it ceases promptly upon its correction or removal. The fact, however, that in many pregnant women the presence of similar lesions is not associated with serious vomiting would apparently indicate that its reflex origin is quite exceptional, and suggest that some other etiological factor is usually concerned in its production. At the same time, the justification for the recognition of this type of

vomiting is afforded by those instances in which prompt cure follows the correction of the abnormality, while the failure of suggestive treatment and the lack of evidence of serious changes in metabolism make it improbable that the affection is neurotic or toxemic in origin.

In the neurotic variety the vomiting is apparently dependent upon the existence of a neurosis—more or less closely allied to hysteria—which may occur in women who had manifested no signs of impaired nervous control previous to the occurrence of pregnancy. In such cases careful examination will fail to reveal the existence of a single physical condition which could account for the vomiting, while the most accurate chemical analysis of the urine will afford no evidence of serious metabolic disturbance; and, finally, characteristic lesions will not be found at autopsy in the rare cases which end fatally, as such patients die from starvation.

Moreover, the neurotic nature of these cases is clearly indicated by the fact that cure frequently follows the employment of perfectly useless remedies and unphysiological procedures, such as a vigorous lecture on the part of the physician, dilating the cervix, or the application to it of various medicaments, applying leeches to the epigastrium, the employment of an exhausted electrical battery, or the administration of an anesthetic, etc. Still more convincing evidence is afforded by the fact that even the most obstinate cases of this character may be cured in a few days by instituting a rigorous rest cure in a well-conducted hospital; while less severe cases yield to suggestive treatment at home, if the patient's family are excluded from the room and the physician is sufficiently positive in his assurance that a prompt cure can be effected.

Toxemic vomiting, on the other hand, is a very serious disease, and is a manifestation of a profound disturbance of metabolism, of the exact origin of which we are ignorant. All that we know at present is that it usually ends in death, and sometimes leads to a fatal termination within a few days after the appearance of serious symptoms. In such cases the patient presents signs of a profound intoxication, and may die in coma without any evidence of starvation. In the last stages of the disease the vomited matter presents a coffee-ground appearance and is expelled without apparent effort.

The urine, while diminished in amount as the result of the scanty intake of fluids, does not contain albumin or casts until shortly before death, and may apparently present a normal amount of urea, as determined by the Doremus method, so that its casual examination gives no clue to the gravity of the condition. In reality, on the other hand, more detailed chemical examination at an early period reveals changes which are indicative of a profoundly altered metabolism. These consist in a decided decrease in the amount of nitrogen excreted as urea, and a marked increase in the amount

put out as ammonia. Accordingly, while the total nitrogen output may be practically normal, the percentage of nitrogen eliminated as ammonia is greatly increased, and this so-called ammonia coefficient, instead of being 4 or 5 per cent. as in normal pregnancy, may rise to 20, 30, or 40 per cent., or even as high as 47 per cent., as in one of the cases reported in my previous article. Moreover, the proportion of amido-acids is increased, but we have not found crystals of leucin and tyrosin, as reported by Ewing in several instances. In some cases the acetone content is abnormally large.

Unexpected lesions are likewise found at autopsy, and Stone, Ewing, Straus, McDonald, and I have observed pronounced changes in the liver and kidneys. The former are closely allied to those occurring in acute yellow atrophy of the liver, and consist in the almost total destruction of the central portion of the liver lobules, the cells of which eventually become necrotic; while the cells in the midzonal and peripheral regions undergo marked fatty degeneration, so that only a few cells at the extreme periphery of the lobule retain a perfectly normal appearance. In the kidneys marked degenerative changes, sometimes amounting to necrosis, are likewise observed, especially in the convoluted lobules.

In view of the clinical history of such cases, and particularly of the characteristic urinary and autopsy findings, it is apparent that one has to deal with a condition totally different from that observed in the reflex and neurotic varieties, and that, therefore, it may be appropriately designated as toxemic vomiting.

In my monograph, I pointed out the extreme importance of differentiating the three varieties, both from the standpoint of prognosis and treatment. Accordingly, it is most essential in every case of serious vomiting of pregnancy to make an extended urinary examination and determine the total nitrogen and the ammonia coefficient. In my experience, if the latter exceeds 10 per cent. the diagnosis of toxemic vomiting should be made and the pregnancy immediately terminated, as there is apparently no likelihood that the process can be checked by therapeutic measures if it once leads to the production of the characteristic hepatic lesions. On the other hand, if the ammonia coefficient is approximately normal the probability of a serious toxemic condition can be eliminated, and the diagnosis will lie between the reflex and neurotic varieties; the latter should be diagnosticated unless some manifest lesions exist in the generative tract.

Likewise, too much stress cannot be laid upon the fact that it is not permissible to make a diagnosis of neurotic vomiting until the possibility of the existence of the toxemic variety has been eliminated by a careful urinary analysis; as in my experience, women suffering from the two conditions may appear equally sick as far as clinical symptoms are concerned. Consequently, the failure to

detect the toxemic character of the disease at an early period may result in the death of a patient, who might have been saved had the condition been recognized and abortion promptly induced.

Since writing my article last year, I have observed three additional cases of toxemic vomiting, which have served to confirm still more strongly my views concerning the radical difference between toxemic and neurotic vomiting, as well as the value of a high ammonia coefficient in diagnosticating the former. Upon this occasion, I desire to report these cases briefly, and afterward to discuss their bearings upon the question of diagnosis as well as upon the nature of toxemic vomiting:

CASE I.—*Serious vomiting in two consecutive pregnancies—toxemic in the first and neurotic in the second.*

Mrs. M. S. (2310 and 2519), a twenty-five-year-old nulliparous patient, was admitted to the medical wards of the Johns Hopkins Hospital, September 10, 1905, having been sent by her physician with a diagnosis of catarrh of the stomach.

Previous to an attack of acute indigestion early in July she had been perfectly well, but from the latter part of that month until September 14th, when she was transferred to the obstetrical department, she had suffered greatly from nausea and vomiting, and had lost considerably in weight. On August 31st she vomited a teacupful of blood, and for several days afterward the vomitus was blood-stained. For some days before admission, and during her entire stay in the medical ward, she vomited every thing she ate, and was rapidly losing ground.

A provisional diagnosis of gastric ulcer was made, and the patient was about to be transferred to the surgeons for operation, when one of the medical men suggested that she was possibly pregnant, and in view of our work upon vomiting, thought that it might be interesting to determine the ammonia coefficient of the urine. This was estimated at 31 per cent. by the resident obstetrician, Dr. Goldsborough, and as the uterus was enlarged and soft and corresponded in size to a two and a half months' pregnancy, he diagnosticated toxemic vomiting.

Accordingly, on September 14th, she was transferred to the obstetrical department, where all feeding by the mouth was stopped and nutrient enemas and large quantities of salt solution administered per rectum. The vomiting, nevertheless, continued and upon several occasions contained considerable quantities of blood. As the patient's condition was gradually growing worse the induction of abortion was deemed advisable, and was attempted on the evening of September 18th under ether anesthesia. The cervix, however, was so rigid that it could not be dilated by Hegar's or Goodell's dilators; accordingly, it was packed with sterile gauze and the patient was put back to bed. By noon the following day it had become so softened that it was readily dilated sufficiently to admit the index

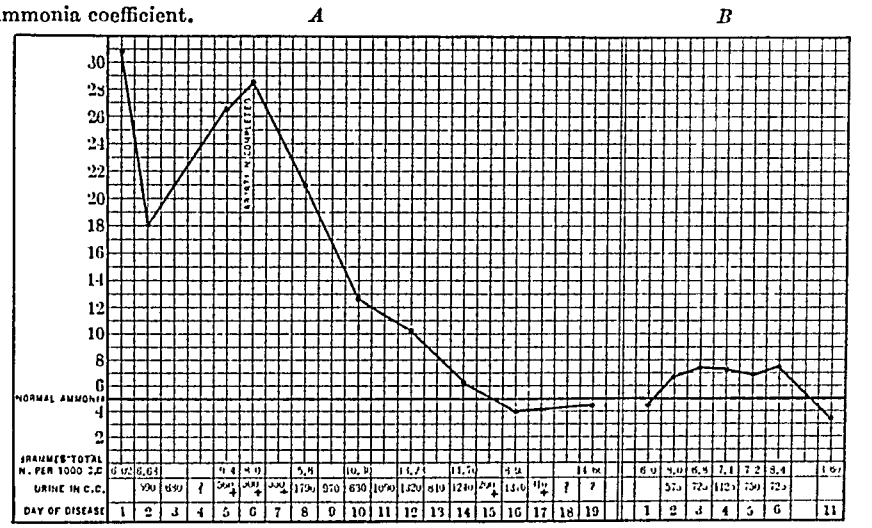
finger, after which the fœtus and its membranes were removed by ovum forceps.

The patient made an uninterrupted recovery, the highest temperature being 100.5° F. She did not vomit again after the operation, and twenty-four hours later expressed a desire for food, which she ate with relish. She gained rapidly in weight and left the hospital on October 3d in perfect condition.

Chart 1, *A*, gives a graphic picture of the rapid return to normal of the ammonia coefficient. It is interesting to note that the urine at no time contained albumin or casts.

The patient returned to the hospital, March 10, 1906, and stated that she was again suffering from vomiting of pregnancy. The last

CHART 1.



CASE I.—Serious vomiting in two consecutive pregnancies—toxemic in the first (*A*, No. 2310, September 14 to October 2, 1905) and neurotic in the second (*B*, No. 2519, March 9 to 19, 1906).

menstrual period was January 17, 1906, and the vomiting had appeared on February 11th, and had been pretty constant ever since.

Examination showed that she was two months pregnant. She was paler and thinner than when she left the hospital in October and was evidently very nervous about her condition. She stated that for the past two weeks she had not been able to retain milk or any solid food, though she did not vomit other fluids.

As the urinary examination was negative, the ammonia coefficient varying between 3 and 7 per cent., a diagnosis of neurotic vomiting was made (Chart 1, *B*). The patient was put to bed, placed upon liquid diet, given no medicine, and was assured that she would recover promptly without the necessity of inducing abortion. After this

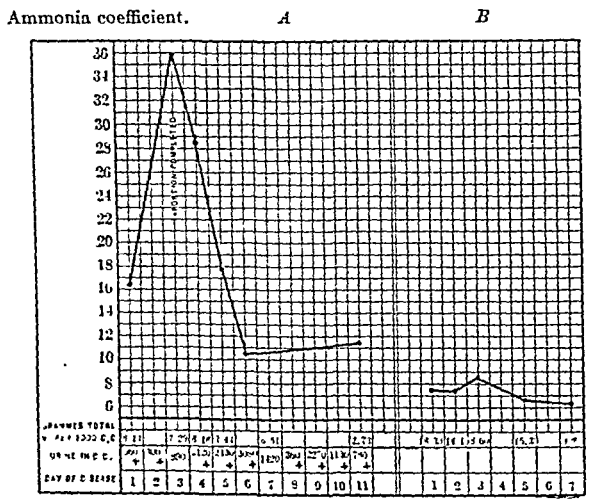
she only occasionally suffered from nausea, which soon ceased entirely, and within a few days she was able to enjoy a full ward diet and left the hospital perfectly cured at the end of ten days.

CASE II.—*Serious vomiting in two consecutive pregnancies—toxemic in the first, neurotic in the second.*

MRS. M. S. (2317 and 2524) was admitted to the hospital, September 20, 1905, at the request of her physician, Dr. C. N. Athey, with a diagnosis of pernicious vomiting of pregnancy.

She was a twenty-one-year-old nullipara, who had menstruated last in May, 1905. Nausea appeared shortly after the non-appearance of the June period and continued ever since to a greater or less degree. For ten days prior to admission she vomited even the blandest fluid

CHART 2



CASE II.—Serious vomiting in two consecutive pregnancies—toxemic in the first (*A*, No 2317, September 21 to October 2, 1905) and neurotic in the second (*B*, No. 2524, March 16 to 23, 1906).

as soon as taken, and has gone down hill rapidly. She was treated by Dr. Athey for several days, but as she vomited every thing taken by the mouth, and could not retain rectal enemas, he advised her removal to the hospital.

On examination she gave the impression of being seriously ill, with lips dry and cracked, eyes somewhat sunken, pulse 120, but of fair volume and tension. The uterus was enlarged to the size of a four or five months' pregnancy. No other abnormalities were noted.

Immediately after admission she was put to bed, given nothing but cracked ice by the mouth, and received 400 c.c. of salt solution per rectum, as well as a nutritive enema every eight hours.

Chemical examination of the urine showed 17 per cent. of ammonia. In view of this and the fact that the symptoms grew worse in spite of two days' treatment, the induction of abortion was determined upon. Accordingly, a medium-sized bougie was introduced into the uterus on the 22d. Upon its removal later in the afternoon the cervix was found to be soft, and under ether anesthesia was readily dilated sufficiently to admit the index finger. The membranes were then ruptured and the fœtus and placenta removed piecemeal by ovum forceps and the uterus washed out with sterile salt solution.

The patient made an uninterrupted recovery and vomited but once after being put back to bed. She asked for food the morning after the operation, and was discharged twelve days later in excellent condition.

As shown by Chart 2, *A*, the ammonia coefficient reached 37 per cent. the day of the abortion, but rapidly fell to 10 per cent. four days later. At no time did the urine contain albumin or casts.

The patient was readmitted March 15, 1906, when she was found to be between two and three months pregnant; last period January 11, 1906. She had been perfectly well up to March 7th, when without any known cause she began to vomit a greenish fluid. Since then she has rejected every thing she has eaten and has vomited almost continuously day and night.

On admission the patient was extremely nervous and very anxious about herself. She had not taken food of any description for two days. The pulse and temperature were normal. She was immediately put to bed and placed upon rectal feeding, and she was earnestly assured that her condition was not serious.

The urinary examination was negative and the ammonia coefficient was 6 to 8 per cent. (Chart 2, *B*). Vomiting ceased after the first twenty-four hours; the next day she asked for food and was put on a soft diet, the enemas being discontinued. She steadily improved and left the hospital one week after admission in excellent condition without having taken a dose of medicine of any kind. One month later she reported that there had been no recurrence.

CASE III.—*Toxemic vomiting of pregnancy.*

Mrs. E. C. (2351), a thirty-one-year-old III-gravida, was seen in consultation, October 13, 1906, when I obtained the following history: Married seven years. Spontaneous labor in March, 1901, the child dying three days later from hemophilia. Suffered intensely from nausea and vomiting during the first half of gestation.

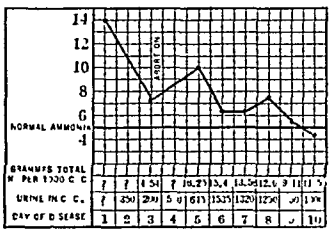
The second pregnancy began in October of the same year, and was marked by still more severe vomiting than before. It became more intense during the fifth month, when she vomited large amounts of coffee-ground material without apparent effort. A few days later she suddenly became jaundiced and profoundly comatose, and her condition was so serious that Dr. Haven, of Boston, who

delivered her by accouchement forcé, despaired of a favorable outcome. She, however, made a satisfactory recovery, and has been perfectly well until the present illness.

The last menstrual period preceding her third pregnancy began August 26, 1905, and morning sickness appeared on October 1st. At the end of a week it had become so severe that she was constantly nauseated and vomited every thing she took. When I saw her on October 12th she was tossing from side to side in bed, vomiting small quantities of clear fluid at frequent intervals, and complaining of intense headache. She had not slept for several nights, and impressed me as being seriously ill. Her face was drawn and haggard, and the pulse varied between 100 and 110, while the temperature was normal.

I at once ordered a twenty-four-hour specimen of urine saved, and in the meantime did not attempt to feed by the mouth, but relied upon rectal enemas. This had no effect upon the vomiting, nor did suppositories of codein and hyoscyamus relieve the nervous condition or induce sleep.

CHART 3



CASE III.—Toxemic vomiting of pregnancy (No. 2351, October 15 to 24, 1905)

The report upon the urinary analysis, which was received on the 15th, showed an ammonia coefficient of 14 per cent., a few hyaline casts, but no albumin. In view of this, together with the history of the previous pregnancy, I regarded her condition as very serious; but as she was decidedly opposed to any interference, I determined to await developments before urging the induction of abortion. I did not have to wait long, as the next day the vomited matter became blood-stained, and she complained of intense pain in the hepatic region, but presented no jaundice. I accordingly urged the necessity for immediate interference, and sent her to the Johns Hopkins Hospital on the morning of the 17th.

Under ether anesthesia the cervix was easily dilated sufficiently to admit a finger, and the uterus cleaned out with ovum forceps and a dull curette.

The nausea and vomiting persisted for two days following the operation, after which recovery was uneventful, the highest temperature being 99.5° F.

I saw the patient again on January 8, 1906, when she desired to know if it would be safe for her to become pregnant again, as she was most anxious for a child. In view of the serious condition in the last two pregnancies, I carefully investigated the hepatic function and found that 100 grams of levulose could be taken without giving rise to insufficiency; while a twenty-four-hour specimen of urine showed 7.84 grams of total nitrogen and an ammonia coefficient of 5 per cent. Accordingly, I stated that I could find no reason to forbid the possibility of pregnancy, though I naturally declined to express an opinion as to its outcome.

The three cases here reported are of very considerable interest in themselves, but when taken in connection with the four cases of toxemic vomiting described in my monograph, they are of the greatest possible value in establishing the diagnostic value of a high ammonia coefficient and its importance as an index to treatment.

Cases I and II demonstrate as clearly as possible the difference in metabolism in the toxemic and neurotic varieties of vomiting. Both patients presented a high ammonia coefficient in their first, and a low one in their second, pregnancies. The first illness was most serious and demanded the interruption of pregnancy, while the second was of but slight importance and yielded readily to suggestive treatment, without the use of medicine. Nevertheless, both patients considered themselves seriously ill when they returned to the hospital for the second time, and had we not been able to differentiate between the toxemic and neurotic conditions by means of the urinary examination it is scarcely probable that we could have been so convinced of the neurotic nature of the second illness as to permit us to assume the authoritative tone so necessary to success in suggestive treatment.

These cases are likewise of importance as showing that toxemic vomiting does not necessarily recur in subsequent pregnancies, and that the hepatic lesions, which we assume accompany it, are capable of repair, or at least do not always lead to serious impairment of function, provided pregnancy is promptly terminated.

Case III, on the other hand, is not so encouraging, for, as far as we can judge from the history, the second pregnancy was complicated by toxemic vomiting, or possibly by acute yellow atrophy of the liver, while there can be no doubt as to the nature of the illness just described. Such a recurrence would apparently indicate that even after a period of three and a half years an anatomical lesion, or at least a predisposition to serious disturbance of metabolism, had probably persisted. But whatever may have been the case in this particular instance, our experience in Cases I and II has clearly demonstrated that recurrence is not universal; and possibly further observation may show that, just as in eclampsia, one attack confers an imperfect immunity in subsequent pregnancies.

From the observations just adduced, I feel that the evidence at present available clearly demonstrates the diagnostic value of a high ammonia coefficient; and whenever it rises appreciably above 10 per cent. in a woman suffering from pernicious vomiting of pregnancy, it indicates a serious disturbance of metabolism, which demands the prompt termination of pregnancy, in the hope of interrupting the process before the organic lesions have become so developed as to preclude the possibility of recovery.

At the same time I do not wish to be understood as contending that a high ammonia coefficient can only occur in this condition, as I know perfectly well that such is not the case.

Several of my friends have suggested that possibly the condition of the urine might be merely a manifestation of starvation resulting from the incessant vomiting, as Folin and Möner have noted corresponding changes in cases of starvation not associated with vomiting. The plausibility of such a contention must be admitted, and one is obliged to confess that its direct refutation is very difficult. Nevertheless, it seems to me that very strong negative evidence is afforded by clinical observation. Thus, one may see two women, both of whom are apparently equally ill and actually suffering from starvation as the result of absolute inability to retain nourishment of any character, and yet one will present a high and the other a low ammonia coefficient. This being the case it would seem very unlikely that starvation could be the only factor concerned.

In view of the fact that chloroform was used as an anesthetic in several of my previously reported cases, which ended fatally, the question arises as to whether some of the symptoms at least might not be attributed to an acid intoxication following late chloroform poisoning, as in several of the cases recently reported in the literature. Such a possibility must be considered, but is most unlikely, as in the three cases here reported, ether was the anesthetic employed.

Dr. C. G. L. Wolf, of the Cornell Medical School, in a recent article upon toxemias of pregnancy, has suggested that the urine of stout women is particularly prone to present a high ammonia coefficient, which should be attributed to abnormal fat metabolism, and has ventured to suggest that such was the case in some of my observations. No doubt he is quite correct in his general statement, but some other cause must be invoked to explain the high ammonia coefficient in most of my cases, as five of my seven patients were thin or emaciated, and only two well nourished, though neither of them could be designated as stout.

While it is possible to speak thus positively concerning the diagnosis of toxemic vomiting, I regret that I am unable to throw further light upon the ultimate nature of the condition than in my previous article.

I have already referred to the liver lesions noted at autopsy, and

the evidence as to their frequency and constancy is rapidly accumulating. In addition to the twelve cases collected in my article, which include those observed by Stone, Ewing, and myself, similar observations have been made by McDonald and Strauss during the past few months. Notwithstanding this, however, we are not in a position to state positively whether the metabolic changes result directly from the liver lesions or represent an attempt on the part of nature to neutralize an acid intoxication, or whether we have to deal with some other process concerning whose nature we are as yet absolutely ignorant.

Personally, I believe that the lesions in the liver are not the primary factor, but result from the circulation of some substance in the blood which has already caused the metabolic disturbance. This view, of course, does not preclude the possibility that the development of such lesions may still further accentuate the existing metabolic abnormality.

The practical identity of the hepatic lesions, as well as the similarity in the clinical history of toxemic vomiting and acute yellow atrophy occurring in pregnancy, force one to the conclusion that the two processes are closely related, if not identical. Thus far I agree with the teachings of Ewing, Stone, McDonald, and Strauss; but I cannot follow them in holding that the conditions just mentioned as well as the pre-eclamptic toxemia, eclampsia, and various other abnormalities of pregnancy, are merely modifications of one and the same toxemia.

At first glance it might appear that such an assumption would simplify matters and lead to their more ready comprehension by physicians in general. To my mind, however, such a belief is absolutely erroneous, and can result only in still further confusion in a field which is already sufficiently dark and complicated. To my mind pre-eclamptic toxemia and eclampsia differ as markedly from toxemic vomiting and acute yellow atrophy of the liver as lobar pneumonia differs from acute miliary tuberculosis No doubt the clinician may occasionally confuse the two conditions, and designate as eclampsia acute yellow atrophy which has resulted in death in coma and convulsions. Such a mistake is perfectly comprehensible at the bedside, but it is without justification in the autopsy-room, as a careful study of the specimens will reveal lesions which are absolutely different.

In eclampsia and pre-eclamptic toxemia, one finds perfectly characteristic lesions, which are thrombotic in character and originate in the portal spaces; while in toxemic vomiting and acute yellow atrophy one finds necrotic lesions in the central or midzonal areas of the liver lobules. The changes in eclampsia are thoroughly characteristic, so much so that I should not hesitate to diagnosticate it whenever I found them, no matter what the clinical history. On the other hand, convulsions, while usual, do not always occur

in eclampsia. Schmorl has described characteristic eclamptic lesions in women dying in coma without convulsions, and I have seen two similar cases.

Moreover, when one takes into consideration the clinical history and the urinary findings in the two conditions, the case becomes still more convincing. In pre-eclamptic toxemia there is usually marked evidence of renal impairment, with scanty urine, casts, and albumin, and usually œdema, and the same generally holds good for eclampsia. In toxemic vomiting, on the other hand, the apparent urinary changes are in the background and the characteristic manifestations are in the nitrogenous partition of the urine and in the profound nervous involvement. Moreover, in eclampsia, in my experience, a high ammonia coefficient usually indicates a favorable outcome, while in toxemic vomiting it is of most ominous prognostic significance.

While we must admit that our information concerning all of these conditions leaves a great deal to be desired, we, nevertheless, know something of them. On the other hand, we occasionally meet with conditions about which we know absolutely nothing. Thus, during the last three years, I have seen several women a day or so after delivery pass into coma, in which they remained for several days, and then gradually recovered, without having had a convulsion. The urine did not contain albumin or casts, and careful chemical examination failed to show any serious derangement in the nitrogenous partition.

The most natural inference is that they were due to a toxemia of some kind, but I do not believe that the cause of science will be served by grouping them into a single class with the other toxemic affections. What we desire to learn is something more as to the true nature of such conditions, and to my mind, advance will only be delayed if such a classification is adopted. I feel that there is no more justification for so doing than to attempt to place all varieties of septicemia in a single group; and surely no one would advocate such a retrograde step.

I believe we should recognize that there are various toxemias of pregnancy, and while we know something about several of them, it is possible that other varieties exist of which we know absolutely nothing at present. Accordingly, the only means by which we can hope to advance is by grouping our cases together according to their anatomical and chemical characteristics, and by waiting for the future to show us the significance of those conditions about which we now know little or nothing, in the hope that we may eventually learn how to classify them.

II.

ELEPHANTIASIS NERVORUM OF THE SCALP: A MANIFESTATION OF VON RECKLINGHAUSEN'S DISEASE.

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AND
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The wisdom of designating maladies, or some of their essential features, by the name of the investigator who first called particular attention to them is contestable. Occasions arise, however, when it is not only a deserved tribute, but a matter of convenience as well. There are few instances in which an individual's name is thus more appropriately linked with a condition of disease than is von Recklinghausen's, for it was he who first demonstrated the histogenetic unity of the morbid changes underlying what had before been considered a number of diverse processes, many of which, owing to their striking and obtrusive nature, had long been known and described under a number of terms. A majority of the terms thus introduced have been descriptive of one or more of the kaleidoscopic features of the malady which now by common consent bears von Recklinghausen's name, but no one term as yet proposed seems to have received general acceptation, generalized neurofibromatosis possibly being as satisfactory as any.

This disease, which, as Feindel has said, is "congénitale toujours, héréditaire souvent, et quelquefois familiale," has for its most constant features certain skin manifestations. These consist chiefly of points or patches of pigmentation, of multiple isolated superficial tumors (molluscum fibrosum), and occasionally of large diffuse growths. In addition to these surface lesions, or indeed in their total absence, there may be multiple tumors distributed along the course of a single nerve or even involving the branches of an entire plexus. These neuromas are often palpable under the skin, but in spite of their size and multiplicity they rarely give rise to pressure phenomena by interrupting the transmission of nervous impulses unless they develop from the nerves during their intraspinal or intracranial course, when compression disturbances of various kinds may arise. Then there occur many so-called symptoms of a secondary order, the evidence of which is less objective: vague sensory disturbances, simple-mindedness, deterioration in mentality, epilepsy, etc.

The patient whose condition we wish to record presented, in addition to many of the commoner features of the disease, a rela-

tively unusual type af diffuse, superficial tumor formation, and the growth, occurring as it did upon the side of the head, was so unsightly that it brought him to the hospital for surgical treatment. Not until we inquired into the matter did we learn that this is by far the more common site of development for these tumors, and the finding has led us to bring together a number of these cases and to present them as a background for our own, the history of which is as follows:

FIG. 1

Front view of the patient, showing deformity of the scalp; also areas of pigmentation and other skin lesions over the body.

Thomas P., aged nineteen years, an American, a laborer, was referred to us by Dr. L. P. Hamburger in November, 1905. His complaint was "drooping of the scalp."

Family History. His parents, three sisters, and three brothers are living and well. He is unaware of the existence of any similar trouble in any member of the family, and thinks none of them have any cutaneous blemishes whatsoever.

Personal History. He has always enjoyed good health, and does not recall any of the diseases of childhood. As long as he can

remember he has had areas of brown pigmentation and numerous small soft tumors distributed over the body. He does not think that any new ones have appeared during the last few years. It was ascertained from the patient's mother that upon the left temporal region, the seat of the present growth, a large "brown spot" had been present for several years before the skin began to sag. She could not tell whether or not it had been present at birth.

FIG. 2

Side view of the patient, showing displacement of the ear and the outer canthus of the eye

When seven years of age, while playing in the street, he was run over and was struck by the horse's hoof, on the left side of his head. The skin was not broken, but the scalp was severely bruised.

About a year after this injury the patient thinks the present tumor began to develop. No subjective symptoms accompanied the growth, and as a matter of fact his attention was first drawn to it by his friends, who noticed that his left ear was becoming somewhat lower than the right. This drooping of the ear and sagging of the scalp during the next four years progressed quite rapidly, so much

so that the scalp covered part of the left cheek, and the ear stood out at right angles from the head. For the past seven years the patient thinks the growth has been slower. At no time has there been pain or sensory disturbances of any sort associated with this growth. He thinks that hearing in the left ear has become slightly impaired.

Physical Examination. The patient is a listless, undersized young man, who would be taken for a boy of fourteen rather than for a person of his real age. His face is not indicative of a high order of mentality. Although he has attended school, he has never learned to read or write.

On the left side of the head (Figs. 1 and 2), extending from the external margin of the orbit to the occiput, and from a point 2 cm. from the sagittal suture to the left external auditory meatus, there is a soft flabby tumor mass which hangs down from the crown, carrying all of the superficial structures with it. It is very readily movable and slides freely over the underlying bony surface without any evident attachment whatsoever. Palpation of the mass imparts the peculiar sensation which Valentine Mott has likened to a relaxed and emaciated mamma. The scalp sags down over the cheek, so that about one-half of it is covered by hair. The skin of the forehead has been drawn down over the external angular process, carrying the outer canthus with it, partly closing the palpebral cleft, and giving the opening a decidedly downward tilt. Over the crown of the head the tumor is less freely movable than in its more dependent portions. It forms on the side of the face a fold extending from the outer margin of the orbit back to the external auditory meatus. The ear has been crowded so far downward that the tip of the pinna is on a level with the lobe of the opposite ear; it has also been displaced slightly backward, and instead of being parallel to the side of the head the pinna stands out perpendicularly to it. Just above the ear there is a large mass within which several knotted cords can be palpated. The tumor is so freely movable that by picking up a large fold of the redundant tissue over the parietal region and pulling it upward and backward the face can be restored almost to its normal outline. The scalp over the tumor is greatly thickened, its surface roughly papillated, and in several areas covered by patches of brownish pigmentation. The hair over the tumor is thinned out and in many follicles only short broken stumps of coarse hair are to be seen. Many of these hairs are without pigmentation. The patient's beard has not as yet developed; merely a few downy hairs are to be seen.

There seems to be some slight atrophy of the temporal muscle under the tumor with relaxation of its fascia, for the index finger can be readily introduced for some distance behind the zygoma. Posterior to and somewhat below the level of the ear are two smaller tumors having the same brownish color and the same consistency

as the larger tumor mass. They measure about 3 x 4 and 2 x 3 cm. respectively. During the examination slight spasmodic twitchings of the facial muscles were seen to occur.

Over the thorax and abdomen the skin shows a variety of lesions. Scattered quite profusely over the trunk, and the extremities as well, are small areas, pin-head in size, of brownish pigmentation. There are also larger patches of pigmentation of irregular outline (Fig. 1), the larger ones occurring upon the chest, the smaller ones scattered over the body, even upon the hands and fingers. There are no patches upon the palms. There is no evidence of segmental distribution in the topography of these patches. Especially over his chest and flanks are scattered numerous slightly

FIG. 3

FIG. 4

The condition after preparation for operation, to show drooping of the scalp, with displacement of the ear and the outer canthus, and replacement of these on gathering up a fold consisting of the main part of the tumor growth.

elevated bluish discolorations, resembling minute bruises. Over the chest and back also are numerous so-called spider angiomas. Many small moles, both sessile and pedunculated, are scattered over the body. His back in particular is peppered with these small growths. Finally, on the chest, one arm, and one leg are a few characteristic soft fibromas. These latter tumors are all of the same general character, of a brownish color, slightly raised above the surface, soft and compressible, giving the characteristic seedless-raisin feeling when examined. They measure on an average about 1 cm. in diameter.

A careful examination of the palpable nerves of the extremities discloses no irregularities in their structure. In only one place

are any definite neuromas of nerve trunks found. These are associated with the large tumor, and will be described later.

Operation under ether November 9, 1905. The accompanying photographs (Figs. 3 and 4) of the patients head were taken by Dr. Gilman, after he had been shaved in preparation for the operation.

After cleaning up the scalp, and while palpating the temporal vessels to determine whether a tourniquet could be so applied as to shut off the extracranial blood supply, the operator found a nodule the size of a bean lying just above the zygoma in front of the ear, evidently upon the auriculotemporal branch of the fifth nerve. Above this nodule could be felt a chain of others, running out into the tumor mass. Consequently, before attacking the tumor proper an incision was made over this region and the primary nodule, while the secondary ones lying above it were dissected out, the temporal artery being ligated at the same time. The tissues were found to be soft, almost gelatinous, and exceedingly vascular, so that some difficulty was experienced in checking hemorrhage even in this small wound. It was closed by deep mass sutures.

The flap of scalp which was to be removed was then pulled up so as to restore slightly more than the natural position of the ear and the horizontal position of the palpebral cleft. A tourniquet was then applied, holding the scalp in this position. The proposed area of tissue for removal was then marked out with the scalpel by a superficial scratch through the epidermis. The incision extended from a point near the external angular process nearly to the occipital protuberance, and included an area of skin on its surface about 15 cm. in cross diameter. It is well that we took this precaution, because from the first deep incision the bleeding was so profuse that had this preliminary step not been taken it is probable that just the right amount of tissue to ensure a successful plastic result would not have been removed, owing to the confusion which the abundant hemorrhage occasioned. As rapidly as possible the incision was carried down through the scalp to the cranial aponeurosis, and as the tissue was dissected away from before backward, the edges of the wound were brought together en masse by a continuous Pagenstecker suture. No vessels were ligated, for we found that the clamps pulled out of the soft tissue by their own weight as rapidly as they were put in. It was only by this taut closure of the wound that we succeeded in controlling the bleeding. The edges of the incision were then more leisurely approximated by interrupted fine silk sutures. No atrophy or change in the bones or the pericranial tissues was disclosed during the operation.

Though the patient lost an amount of blood during the operation sufficient to leave him somewhat anemic for a time, he made a rapid and satisfactory recovery. At one point the sutures in the scalp had failed to check the bleeding completely, so that a small

hematoma formed underneath the edge of the incision. When the sutures were removed some days later this clot broke through and left a point which healed slowly by granulation. The practical restoration of the eye and ear to their normal position is shown in the accompanying photograph (Fig. 5). It is quite possible that there may be a recurrence of the growth, particularly as the two isolated masses resembling the original tumor and lying over the mastoid process were not removed with the spindle-shaped piece of tissue taken away at the operation. For a few weeks after the operation the angle of the eye and the ear were drawn up into a position somewhat higher than on the opposite side, but this overcorrection of the pre-existing deformity has gradually disappeared.

FIG. 5

Postoperative condition, to show restoration of the eye and the ear to practically the normal position

Pathological Findings. The tissues for examination were a neurofibroma removed by a separate incision from just above the left ear, and a diamond-shaped piece of scalp from the left parietal region.

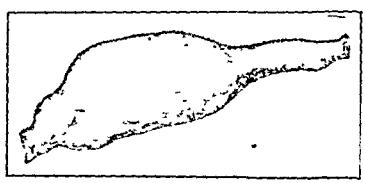
The neurofibroma measured 1.8 x 0.8 x 0.6 cm.; it was soft and elastic, and of a dull-gray color. The surrounding tissue readily stripped from its capsule, leaving a smooth and glistening surface. Toward one end there was a small sulcus which indefinitely divided the tumor into two lobes. The nerve trunk proximal to the neurofibroma was uniformly thickened as far as it had been removed; the nerve distal to the tumor was of smaller diameter, and it emerged

from the main lobe (Fig. 6). On fresh section the tumor was translucent, smooth, rather œdematous, and of a yellowish-gray color. Running through its centre was to be seen a more opaque, whitish band, striated transversely, and at one point sending off a branch into the other of the two lobes. The capsule was everywhere well defined.

Microscopically, the neurofibroma is found to be made up for the most part of a loose connective tissue. It consists of interlacing strands of fibers forming a very fine network, the meshes of which appear almost like vascular spaces. This loose tissue varies considerably in its cellular contents; in some areas it is almost entirely fibrous, and in others very cellular. Through the centre of the tumor there passes a dense band of connective tissue, in the wavy outlines of which the nerve fibres can be demonstrated.

The central strand is made up principally of spindle-shaped cells with large vesicular nuclei. The looser tissues consist of finer drawn-out cells with solid, dark-staining nuclei. Occasionally very large vesicular nuclei are to be seen. There are very few cells of the wandering-cell type, although an occasional group of young

FIG. 6



Sketch of the neurofibroma from the auriculotemporal branch of the fifth nerve. (Actual size.)

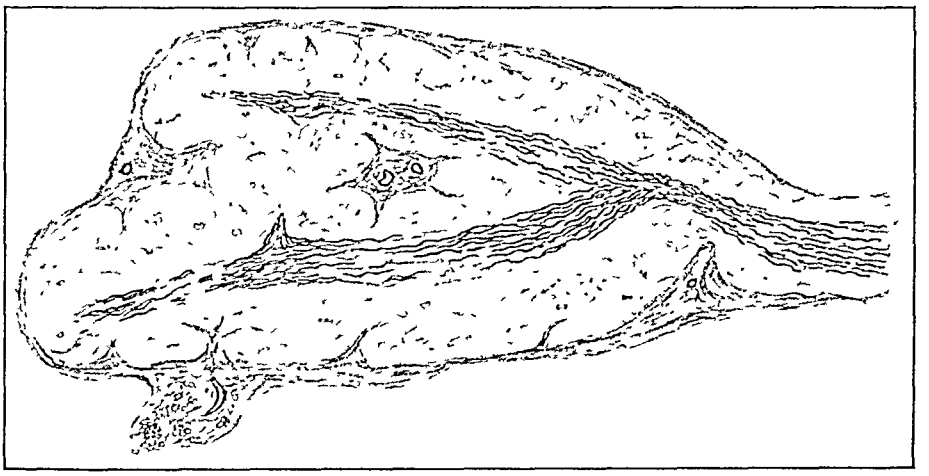
fibroblasts resembles them very closely. Though there are but few vessels in the tumor itself, the vascular supply of the capsule is abundant, and several tags of adherent tissue prove to be of the same type as the tissue which makes up the greater part of the thickened scalp.

With Mallory's connective-tissue stain the central cord stands out very prominently, and among the blue connective-tissue fibers a few yellow-stained nerve fibers can be made out. Sections stained with Weigert's elastic-tissue stain gave negative results. The specific stains used to demonstrate the nerve fibers were Weigert's myelin-sheath stain and Robertson's modification of Heller's stain. The latter stain, on account of its more definite color contrast, was used in the great majority of the preparations. A series of sections taking in the entire diameter of the neurofibroma was stained. The series shows that there are two main strands of nerve fibers running through the tumor mass, about as they are indicated in Fig. 7, which does not represent any one section, but a composite of one near the beginning and one near the end of the series, in

order to bring out in a clearer manner the course of the fibers. As can be seen in the sketch, the greatest part of the tumor is due to a proliferation of the perineural connective tissue, but judging from the distance which separates the individual nerve fibers there has been considerable proliferation of the endoneurium as well. The amount of endoneural thickening varies considerably in different parts of the tumor. The fibers of the entering nerve are quite widely separated, while the nerve leaving the tumor shows some perineural thickening, but the nerve fibers themselves form a compact bundle. The point at which the second band of fibers leaves the tumor corresponds to the small lobe that was made out in the gross. The nerve evidently was cut off short. The individual nerve fibers, both large and small, appear perfectly normal.

Scalp. In its shrunken condition after hardening the portion of scalp removed measured 15.2 x 7.5 cm. Its thickness varied

FIG. 7



Longitudinal section of the neurofibroma pictured in Fig. 6. (Robertson's modification of Heller's stain)

from 0.5 cm. at the periphery to 1.2 cm. in the central areas. The epithelial surface was irregular, due to marked papillary formation about the hair follicles. This was especially apparent in those areas where brownish pigmentation was most abundant. The cranial surface was rather ragged in appearance, and the tissue was quite uniformly soft, œdematous, and of a yellowish-red color. It had a peculiarly flabby feel to it. At the posterior inferior corner of the spindle-shaped piece of tissue there were found several nerves which showed nodular thickenings. One of these thickenings measured 1.4 cm. in length by 0.2 cm. in diameter. These were the only neurofibromas seen on inspection, and are indicated at *a*, in Fig. 8.

The thickening of the scalp was due almost entirely to œdematous connective tissue, which after hardening in formalin was quite

tough and could be readily pulled off in sheets, and sometimes also in small cords that resembled nerve fibers. In the areas of greatest thickening the nerves and neurofibromas were no more abundant than elsewhere.

On cross-section of the scalp the tissue presented a uniform fibrous appearance. The hair follicles were enlarged and extended in some areas three-fourths of the distance through the scalp. About them there was a small ring of fibrous tissue. The bloodvessels that were cut in different sections were not loose in the subcutaneous tissue, and a definite wall could not be dissected out, but were firmly embedded in the fibrous tissue. One vein was cut longitudinally for a distance of about 2.5 cm. It did not collapse, but remained open its entire length, looking like a small trough. In

FIG. 8

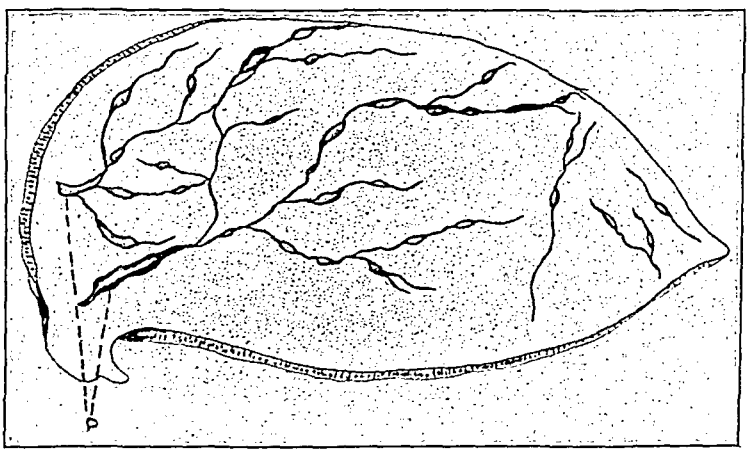


Diagram of the neurofibromas, dissected out in the removed portion of the scalp.

attempting to free it from the surrounding tissue it was torn, but could not be dissected free.

On carefully dissecting out some of the nerve twigs found on the under surface of the scalp numerous small neurofibromas were found. These tumors were all of about millet-seed size, scattered irregularly along the different nerves, as shown in Fig. 8. They were most abundant just beneath the corium, lying between the hair follicles (Fig. 9). The nerve fibers became so fine in this layer that after the cluster of neurofibromas was dissected out it was almost impossible to follow them further. In one instance after a nerve had divided into two branches a neurofibroma on one of its branches, about 0.5 cm. beyond the division, enclosed the other branch as well. The smaller tumors had the same cross-striation that was seen in the central cord of the neuroma described

above at some length. In every instance the neurofibromas, owing to their definite encapsulation, could be readily shelled out from the surrounding fibrous tissue.

On microscopic examination of the scalp the most marked change to be noted is the great increase in cellular connective tissue in the subcutaneous layer. This tissue shows no definite arrangement, but consists of dense, irregular masses, chiefly in the lower layers of the tela subcutanea. In many areas also the normal fibrous corium is replaced by this same cellular connective tissue, which in many spots may extend even as far as the epithelium itself. The tissue consists of fibroblastic cells with relatively large vesicular nuclei, that run in bands, layers, or form an irregular network. Numerous "mast-zellen" are scattered through the connective tissue. The subcutaneous tissue contains a considerable amount of fat, which also has been invaded by the sclerosing process, for the alveoli are separated by thick strands of fibrous tissue.

Sections stained with Weigert's elastic-tissue stain demonstrate very clearly that the portion of the scalp below the corium is relatively free from elastic fibers. Throughout the pars reticularis and papillaris of the corium itself, however, a fine tracery of elastic fibers can be demonstrated. At numerous points small strands of tissue containing elastic fibers extend from the corium for short distances into the subcutaneous tissues. In the tela subcutanea proper the elastic fibers are very poorly developed; only here and there are seen a few small scattered fibers. In the lowest portion an occasional fiber is seen.

The epithelium is normal in appearance, except for its unevenness, which was noted in the gross. Underlying the epithelium the cells contain some yellow pigment, as do also the wandering cells in the spaces of Lange. The corium, except for the invasion of fibrous tissue from below, also appears normal.

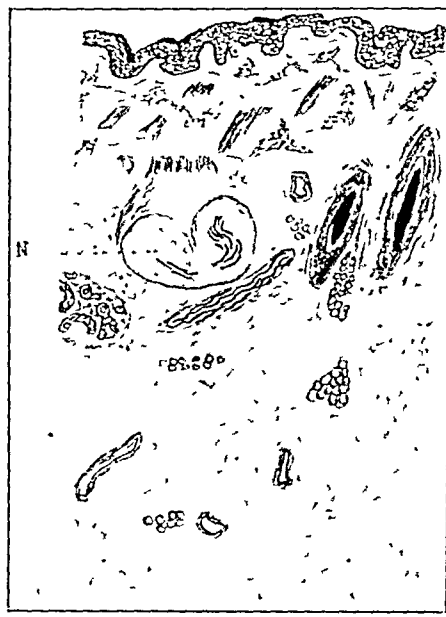
The hair follicles are larger than normal, dipping deep down into the subcutaneous tissue, and the connective tissue about them is increased in amount. The sebaceous glands are also proportionately enlarged. The sweat glands are not increased in size or number, nor are there to be seen any finger-like processes growing into the subcutaneons tissues, such as von Recklinghausen described. The capsules of the glands are slightly thickened.

The lower layer of the subcutaneous tissue is quite vascular. The walls of the vessels do not stand out distinctly, as is the rule in connective tissue, but they are firmly embedded and seem fused with the cellular connective tissue about them. This is especially well seen in some of the larger veins, in which the wall proper cannot be distinguished from the concentrically arranged connective tissue, which at certain points seems almost to make up the entire wall. The elastic tissue in the vessel walls seems normal.

The neurofibromas were very infrequent in the different sections

taken from the scalp, though numerous nerves were seen, showing slight increase in the size of their perineural sheaths. One of these neuromas is shown in Fig. 9. The nerves, as well as the tumors upon them, are definitely separated from the surrounding fibrous tissue, sometimes even by a small interval. Thus, the interlacing fibrous tissue cells of the nerve sheath are quite distinct from the surrounding tissue which possesses the same histological character. The nerve fibers in the small subcutaneous tumors are few and run irregularly through them, so that very probably there has been a proliferation of the endoneurium as well as of the perineurium, a condition similar to that found in the larger neuroma first described.

FIG 9



Miliary neurofibroma in a section of the scalp (Robertson's modification of Heller's stain)

Just why the trigeminal field and the temporal region in particular should be the seat of predilection for these growths is not apparent. Bruns, in his review of these cases, found that more than a third of the so-called "Rankenneuromata" originated in this territory. The tumors are painless, and troublesome only because of their unsightliness and the great size which they may attain. Hence, it is natural to suppose that they will more often lead their hosts to seek surgical relief when they occur upon an exposed part of the body than when they are hidden from sight. But even this does not suffice to account for the great predominance of the temporal cases. They are, furthermore, much more common in men, as the subjoined list indicates.

Only one of the several patients afflicted with von Recklinghausen's disease who have been admitted to the various services at the Johns Hopkins Hospital has possessed an elephantiatic growth of this nature. This was a woman with all the hall-marks of von Recklinghausen's disease, in whom an enormous tumor mass hung from the right side in much the same position and of about the same proportions as in the case depicted by Virchow as a frontispiece to *Die Krankhaften Geschwülste,* vol. i. This, after the temporal region, is perhaps the second most frequent seat of origin for these tumors.

Although these large isolated growths are almost invariably accompanied by other manifestations of von Recklinghausen's

FIG. 10

Valentine Mott's case of "pachydermatocele."

disease, the tumors themselves have come to be designated by a most variable terminology. In his classical monograph, von Recklinghausen himself adheres to the term elephantiasis mollis, used by Virchow. Mott designated the growths pachydermatocele. Verneuil introduced the terms plexiform neuroma and neuroma cylindricum plexiforme. Among other designations are elephantiasis molluscum (Nélaton); rankenneurom and neuroma circoideum (Bruns); dermatolyse (Marie); elephantiasis neuromatodes (Bruns); lappen-elephantiasis (Esmarch); cylindrisches fibrom (Marchand); fibroneuroma racemosum (Rizzoli); tumeur royale (Boudet), etc.

In his monograph von Recklinghausen cites one or two cases which appeared in the literature before 1854, but possibly it may

be well to begin our report with the cases which were recorded by Valentine Mott.

1854. Valentine Mott. "Tumors of Skin Denominated Pachydermatocele," *Med. Chir. Trans.*, London, 1854, vol. xxxvii, p. 155.

Case III of his series. A boy, aged fourteen years, consulted him because of a "hideous deformity" on the right side of his head and face. The tumor formed three layers, extending from the crown of the head to below the jaw. One fold involved the upper eyelid, and when raised revealed the globe at the end of a canal four inches in depth (Fig. 10). The tumor was twice operated upon, but the growth recurred after each operation.

FIG. 11

Billroth's Case of "plexiformes neurofi brom."

Case IV of his series. A boy, aged twelve years, presented a swelling on the right side of the face which began in early infancy and was probably congenital. Its description corresponds exactly to the case cited above. The operation was successful and there was no return of the growth during the following six years.

It is to be noted that Mott limited the description in these cases to the tumor lesion alone, and he makes no reference to the presence of other skin manifestations which we now include under the term von Recklinghausen's disease.

1863. Billroth. "Ueber die Entstehung der Fibroide," *Archiv f. klin. Chir.*, 1863, Band iv, p. 547.

A boy, aged six years, presented a tumor consisting of small,

hard strands and masses overlying the right upper eyelid and temporal region. On microscopic study of the tumor after its removal it was found that there was a central strand, evidently a nerve, which on entering the growth became either fibrous or changed into a soft mass of fat. Its structure could not be clearly made out.

1869. Billroth. "Plexiformes Neurofibrom des oberen Augenlides und der Schläfengegend," *Archiv f. klin. Chir.*, 1869, vol. xi, p. 232.

A boy, aged eighteen years, strong and healthy, of moderate mental development, had had since birth a tumor of small size over the temporal region. It had suddenly taken on a rapid growth unaccompanied by any symptoms of discomfort. It had become as large as a fist, and involved the temporal region and upper eyelid. It was soft and flabby, and extended deep into the orbit. A defect

FIG. 12

Bruns' Case I, "Ranken-neurom."

was found in the parietal bone about the size of a pea. The tumor, which was removed, was seen to consist of a mass of plexiform, grayish-red, smooth, round cords. During the following thirteen months there was no recurrence (Fig. 11).

1870. Bruns. "Das Ranken-Neurom," *Virchow's Archiv*, 1870, vol. l, p. 80.

Case I, a man, aged twenty-eight years, had had since birth a painless tumor in the right temporal region. There was no history of a similar affliction in the patient's family. There were no intellectual disturbances; his general health was good. The tumor was situated just above the right ear, which was so pushed down that the pinna stood out horizontally (Fig. 12). The tumor possessed

a wormy feel, and was of rather soft consistency. It was removed, the patient dying from infection some days later. Microscopic examination showed new formation of nerve fibers by metaplasia of connective tissue.

Case II, a patient, aged thirty-three years, whose brother, Case III, had a similar tumor. The mother had numerous cutaneous wart-like excrescences over her body. Since birth the patient had had a flat tumor involving the left temporal region and left upper eyelid. At the time of puberty the growth developed and the eye had been lost owing to a suppurative infection. There were several painful spots over the tumor. On palpation numerous coils of a firmer consistency could be made out in the soft stroma of the growth.

FIG. 13

Bruns' case II, "Ranken-neurom"

As seen in the illustration (Fig. 13) there was also a large cervical tumor which was removed at operation. The patient died on the tenth day from hemorrhage due to ulceration of the carotid artery.

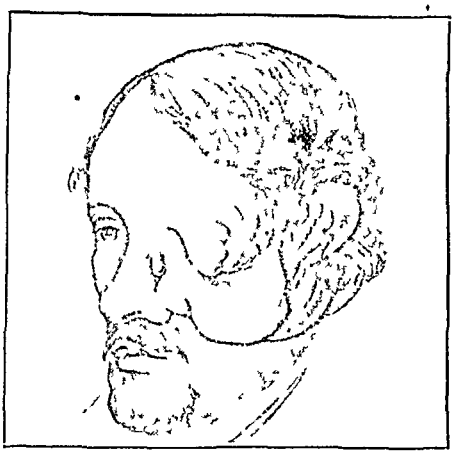
Case III, a man, aged forty-three years, a brother of Case II. This tumor likewise was congenital and resembled very closely the one described above (Fig. 14). The eyeball in this case also had been lost at the time of puberty. There were no local areas of tenderness. The tumor was soft and movable, and on deep palpation numerous so-called cords could be found running through it.

1870. Laroyenne. Christot, *Gaz. hebdom.*, 1870. Ref. Cartaz, *Archiv. gén. de Méd.*

A child, aged five years, healthy in appearance, presented a painless tumor over the right cheek, which had enlarged rapidly shortly

before he came under observation. The tumor was soft and had numerous small palpable thickenings scattered through it. An incomplete operation was followed by immediate recurrence. The

FIG. 14



Bruns' Case III, Ranken-neurom. Brother of Case II, Fig 13.

microscopic characters were those of a plexiform neuroma, showing at many points sarcomatous degeneration.

1870. Rizzoli. *Lo Sperimentale,* November, 1870. Ref. Bruns, *Beiträge zur klin. Chir.*, 1891, vol. viii, p. 1.

FIG. 15

Billroth's case of bilateral involvement of frontotemporal region

Two cases are reported by Rizzoli, one of them a child, aged six years, in whom a tumor growing from the upper eyelid and skin over the orbital arch had been present since early life. In the other

patient, a man, aged twenty years, there had been present since early life a ranken-neurom which had developed in the temporal region and upper eyelid.

1870. Billroth. *Chir. Klinik*, Wien, 1869–1870, 54.

A man, aged thirty-three years, had had since early life a small swelling over the left eyebrow. Later on a similar swelling appeared over the right eyebrow. These tumors had slowly increased in size, forming sac-like folds which hung down over the eyes and cheeks (Fig. 15). After twenty operations the greater part of these tumor masses was removed. The patient had also a few superficial pea-size tumors over his chest.

1873. Fritsche. "Two Unusual Cases of Elephantiasis Arabum," *Clin. Soc. Trans.*, London, 1873, vol. vi, p. 160.

A patient, a beggar, aged twenty-six years, had an elephantiatic transformation of the right half of his face; "the whole side of his face resembled an empty hanging bag." The tumor had been present since childhood. The opening of the right eye was on a level with the nostril. The eyeball was atrophied and hung by a long pedicle, the optic nerve being very near the opening of the eyelids. The helix of the right ear was enlarged and hung loosely down. The patient was said to be otherwise normal.

1875. Stokes. "Pachydermatocele or Fibromolluscum," *Dublin Journal of Med. Sci.*, 1875, vol. lix, p. 69.

A man, aged thirty-two years, had had a slowly growing tumor situated in the temporal region. It had appeared early in life and had grown slowly. His general health was good. The tumor was very movable; its surface was irregular and nodular. It was not discolored, but was thickly covered with hair. An operation was successfully performed, though there is a note of great difficulty from a tremendous hemorrhage.

1876. Billroth. "Geschwülste," *Chir. Klinik*, Wien, 1872–1876.

A girl, aged fifteen years. There had been noticed since childhood a fulness of the right temporal region. In this situation a tumor developed which involved the temporal region and upper eyelid and upper part of the cheek. In the tumor mass numerous hard, irregular cords could be palpated. The tumor was tender. In two operations it was completely removed and there was no recurrence.

1876. Cartaz. "Etude sur le Neurome Plexiforme," *Archiv. gén. de Méd.*, 1876, vol. cxxxviii, p. 176.

A boy, aged eleven years, with a negative family history, had had since birth a tumor, the size of a dollar, elevated about 1 cm. above the scalp. It was situated over the left ear. It had developed slowly until within a few months, when it had doubled in size. It was painless. It hung down over the neck, and in the soft mass could be palpated cords and chains of harder tissue. The operation for its removal, though successful, proved a very bloody one.

1877. R. Marchand. "Das Plexiforme-Neurom (Cylindrische

Fibrom der Nervenscheiden)," *Virchow's Archiv*, 1877, vol. lxx, p. 36.

A boy, aged twelve years, in whom a tumor was first noticed when six months old. The growth was very slow. There was no history of a similar condition in the family. The upper lid of the left eye and adjacent part of the temporal region were involved. The upper lid hung down like a sac over the left eye, but on raising the tumor mass the eye was found to be normal in all respects. On deep palpation numerous dense cords could be made out. Deep pressure elicited some pain. The patient was successfully operated upon and the tumor is said not to have recurred.

Marchand reports the case of a boy aged eighteen years. There had been present since his fourth year a large tumor situated just

FIG. 16

Schuller's case, involving the territory of the superior maxillary as well as the frontotemporal region.

above his right ear. It had slowly enlarged, and at the time of operation consisted of a soft, doughy, painful swelling over the right temporal and occipital regions. In the depths were felt numerous strands of firm tissue on which small enlargements were palpable. The tumor was partially removed by operation.

1878. Schüller. *Deutsche Zeitschrift f. Chir.*, vol. ix, p. 261.

A woman, aged eighteen years, presented a tumor involving the left side of the face. It had developed slowly until puberty, after which time its growth was more rapid. The mass presented the usual characteristics of position and consistency (Fig. 16). It was removed, with a fair cosmetic result. The eyeball had been destroyed by suppuration some time before the operation.

Schüller reports a second case in a woman aged twenty-four years. A tumor on the right side of the face had been present since infancy, enlarging slowly until the time of puberty, when it had rapidly increased in size. In the deeper portions of the tumor several cords and knots could be palpated. It was successfully removed at operation.

1880. Schultze. "Ein Fall von sehr grosser Fibroma Molluscum an Kopf und Gesicht," *Deutsche Zeitschr. f. Chir.*, 1880, vol. xiii, p. 374.

A young man, aged twenty years, had a tumor the size of his head hanging from the temporal region and cheek. It measured 31 x 22 x 12 cm. in its several diameters. There was no family history of a similar condition. The growth was first noticed when

FIG 17

Schultze's case, designated a large "fibroma molluscum"

the patient was four years of age. It was then about the size of a pea. Within a year it grew considerably and was removed. It returned almost immediately and rapidly enlarged to its present size (Fig. 17). A radical operation was done in three stages, with a fair cosmetic result.

This case was studied histologically by von Recklinghausen, who was unable to demonstrate any nerve fibers in the tissue, but he considered this to be due to the enormous size of the growth, which was made up of fibrous tissue at the expense presumably of a few nerve fibers which were not demonstrable. He nevertheless regarded the case as one of "elephantiasis mollis."

1882. Labbé. (Case IV of Bruns' series.) *Beitrage zur klin. Chir.*, 1891, vol. viii, p. 1.

A woman, aged twenty years, had a tumor involving the forehead and upper eyelid, which had been present since she was a year old. The growth hung loosely down in a large fold.

1880. Schuster. (Case XVI of Bruns' series (*loc. cit.*). A boy, aged fourteen years, had an elephantiatic enlargement which had been present since his fourth year. It involved the nose and cheek. The body was covered with numerous areas of pigmentation and fibroma molluscum.

1882. Socin. "Angeborne Elephantiasis der Rechten Gesichtshälfte," *Jahresbericht der Chir.*, Abth. d. Spitals zu Berne, 1882, p. 29.

A woman, aged twenty-seven years, who had always been healthy presented a tumor which had been slowly growing and which covered the right half of the forehead and temporal region, surrounding the orbit like a crescent, and hanging over the region of the upper jaw. It was pigmented, and within the mass could be felt the usual knotted cords. The upper lid was greatly enlarged and hung down over the eye in a large fold. In spite of serious hemorrhage the tumor was successfully removed in two stages.

1883. Volkman. "Beiträge zur Kenntniss vom Plexiforme-Neurom," Dissertation, Magdeburg, 1883.

A boy, aged ten years, had a congenital tumor hanging from the scalp, which reached as low down as the clavicle. The skin over the tumor was pigmented, hypertrophic, and was thickly covered with hair.

1890. Rapok. "Beiträge z. Statistik der Geschwülste," *Deutsche Zeitschr. f. Chir.*, vol, l. S. 538.

A girl, aged seventeen years, showed a tumor which developed in her upper eyelid during childhood. For a year and a half before she came under observation the growth had been much more rapid. Her father also had "neurofibroma plexiforma."

1891. Andry and La Croix. *Lyon Médical*, 1891, tome lxvii, No. 21, p. 109; No. 22, p. 145.

A boy, aged eight years, giving no history of a similar condition in the family, had a tumor which was first noticed when he was two years of age. He was of normal mentality. The growth had been gradual and at the age of eight the tumor, involving the left temporal region and the left upper eyelid, had reached a large size. It presented the usual characteristics. It was successfully removed at operation.

1891. Bruns. "Ueber das Rankenneurom," *Beiträge zur klin. Chir.*, vol. viii, p. 1.

Case VII of his series. A female, aged twenty years, had a tumor of congenital origin, involving the upper eyelid and orbit. The upper lid was greatly enlarged and elephantiatic. There was also a defect in the roof of the orbit.

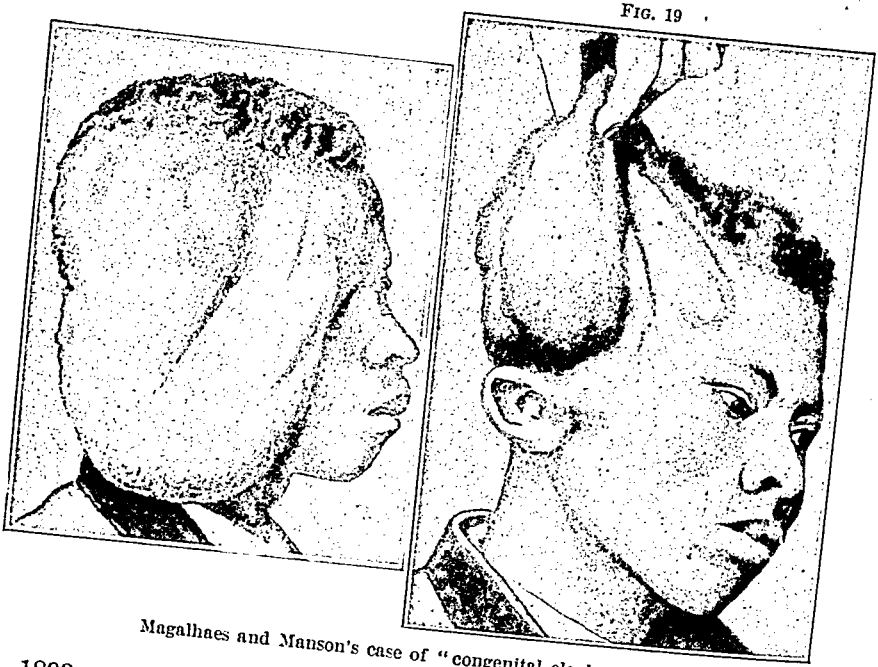
Case XI of his series. A patient of Dessauer's. A man, aged

forty-two years, had a tumor of the temporofrontal region and involving the upper eyelid. There was also a large growth of similar character hanging from the loin. The tumors consisted of several soft flabby folds of skin. Besides these tumors he had numerous nævi and fibroma molluscum.

Case XIV of his series. A man, aged thirty-eight years, had a congenital tumor involving the frontal region and upper eyelid. Hanging from the forehead, the tumor was draped down over the eye in several soft, flabby folds. There were numerous fibromata molluscum scattered over the body.

FIG. 18

FIG. 19



Magalhaes and Manson's case of "congenital elephantiasis."

1893. Magalhaes and Manson. "A Case of Congenital Elephantiasis of the Scalp," AMER. JOUR. MED. SCI., 1893, vol. cv, p. 120.

A man, aged thirty-two years, since childhood had a growth which originated from the right side of the scalp and had slowly and progressively increased in size. The "hood-like" mass was soft and flabby. The right half of the cranium corresponding to the tumor was markedly deformed (Figs. 18 and 19).

1896. Dennis. We are indebted to Dr. Frederic S. Dennis for this photograph (Fig. 20) of a patient whose tumor and other skin lesions are depicted in a more advanced state in vol. iv. of his *System of Surgery*. The condition is associated with the other

manifestations of von Recklinghausen's disease, and the growth was of long standing.

FIG. 20

Dennis' case.

FIG. 21

Lanz's case of "fibroma molluscum."

1904. Lanz. *Handbuch d. Chir.* Bergmann, Bruns, and Mikulicz, second edition, vol. i, p. 31.

A man, aged twenty years, had a large growth (Fig. 21) which

made him look as though he was wearing a pendulous cap. The mobility of the mass was very marked. He had fibroma molluscum and areas of pigmentation scattered over his entire body. The tumor was successfully removed.

1905. Wynn. "Plexiform Neurofibroma," *Jour. Amer. Med. Assoc.*, 1905, vol. xlvi, p. 500.

A young man, aged nineteen years, giving no history of similar affliction in the family, had an elephantiatic tumor of the forehead, which was removed when he was eleven, but which gradually returned. Beginning about the fourth year, there developed a dense, diffuse enlargement over the parietotemporal region, and somewhat later in the orbits and cheek. The skin hung in folds from the orbits down over the lower jaw. Irregular, worm-like masses could be palpated deep in the tumor. Microscopically, no nerve fibers were demonstrated.

ORIGINAL ARTICLES.

GRAPHIC METHODS IN THE STUDY OF CARDIAC DISEASES.[1]

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(From the Medical Service of the Johns Hopkins Hospital.)

The first observations upon pulsation of the veins was reported to the French Academy by Homberg in 1704,[1] in a case of heart failure; Zuliani, in 1805, and Benson, in 1836, noted similar pulsation in cases in which autopsy showed tricuspid insufficiency; and Kreysig, in 1814, observed the pulsating liver in such cases. The experimental study of the pulsation in the veins was first undertaken by Barry in England, in 1826, and by Wedemeyer in Germany, in 1828;[2] but although Weyrich, in 1853,[3] and Bamberger[4] and Friedreich,[5] a decade later, made further contributions to this subject, little practical importance was attached to it. The scientific investigation of pulsations and pressure changes in the circulatory system really dates from the publication of Marey's *Physiologie médicale de la circulation du sang* in 1863, and the careful and complete experimental and clinical studies emanating from his laboratory have furnished the basis for most of the work done before 1895. Since then the work of Engelmann[6] on the myogenic origin of the heart-beat, and its clinical application by Hering[7] and Wenckebach,[8] have given a new stimulus to the study of the diseased

[1] Read before the Johns Hopkins Medical Society, Baltimore, February 19, 1906.

heart from the standpoint of its rhythmicity, irritability, force of contraction, and conductivity.

While this work was being done in the laboratories of Holland and Germany, an English practitioner, James Mackenzie, of Burnley, was working out its clinical application. He made many routine tracings simultaneously from the radial and the carotid arteries, the jugular vein, and over the heart, to discover the sequence and strength of the contractions of the auricles and of each ventricle as well, and to locate the site of the disturbance in function. Mackenzie amassed a tremendous amount of important information; and the appearance of his book upon the *Pulse*, in 1903,[9] may almost be said to mark a new era in the study of cardiac disease.

The observations which I shall present to illustrate the various phases of disturbed heart action were begun in the service of Prof. J. O. Hirschfelder, in San Francisco, in conjunction with Dr. Emil Schmoll, and have been continued in the medical clinic here during the past three months. Owing to improvements in technique and apparatus, all the tracings to be presented this evening, except that in Fig. 15, were made here, although similar results had been obtained in San Francisco.

The apparatus used in San Francisco was simply a Harvard revolving drum, with two Marey recording tambours. This is quite satisfactory, but very bulky. Mackenzie and the German observers use a modified Jacquet sphygmograph, upon which a Marey tambour and recording lever is mounted, so as to give at the same time a tracing from the radial and one from the carotid, jugular, or apex. This apparatus, known as the Jacquet cardio-sphygmograph, is small and portable, but like all radial sphygmographs it is more or less difficult of application, and a great deal of valuable time may be lost in adjusting it.

In the medical clinic here we have been using a modification of the Erlanger blood pressure apparatus,[10*] which has been very satisfactory and which has the advantage of revealing the blood pressure and giving the brachial pulse tracing; it also affords a method of differentiating between certain forms of pulse irregularities that cannot be differentiated by other methods. With this apparatus

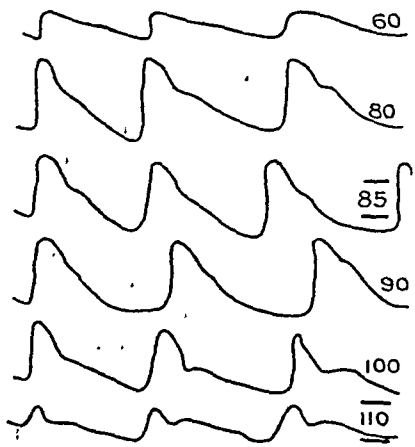
* The clockwork moving the drum of the Erlanger apparatus has been modified so as to give a fast rate of rotation as well as a slow one—and an upright steel rod fixed in the base of the apparatus so as to carry two Harvard sphygmograph tambours to write upon the drum. The exact application is secured by screw adjustments. The recording levers are made of magnesium (flash-light) ribbon; the writing points are of celluloid film, and are very convenient. From the tubes of these recording tambours rubber tubes lead off to the receiving funnels. The most convenient form for the latter is, for taking the jugular pulse, an ordinary stethoscope bell—the open arm of the Y-tube being closed with the finger after the bell has been satisfactorily applied over the vein.

For carotid pulse or apex-beat the soft rubber tip used upon stethoscope bells may be employed. The small end of this is plugged with a perforated rubber stopper, through which a T-tube is inserted, and this is applied as above.

For liver or respiration tracings a medium-sized glass funnel may be used.

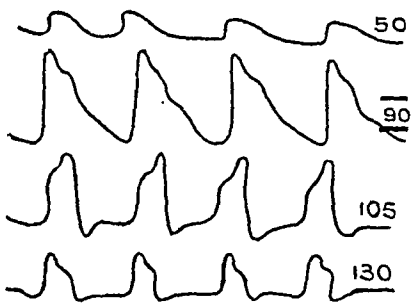
the pulse in the brachial artery is taken, and may be taken at any desired pressure. This is of great importance, as different pressures upon the artery greatly modify the pulse form. This can best be illustrated by a series of brachial tracings from the same artery at different pressures (Figs. 1 and 2), which show why so many good observers can obtain almost any form of pulse with the radial

FIG. 1



Brachial pulse tracings taken from the cuff on the upper arm of a normal individual, with pressure of air in the cuff at 60, 80, 85 mm. (diastolic pressure), 90, 100, and 110 mm. Hg (systolic pressure) respectively, showing the change in pulse form due to pressure on the artery.

FIG. 2



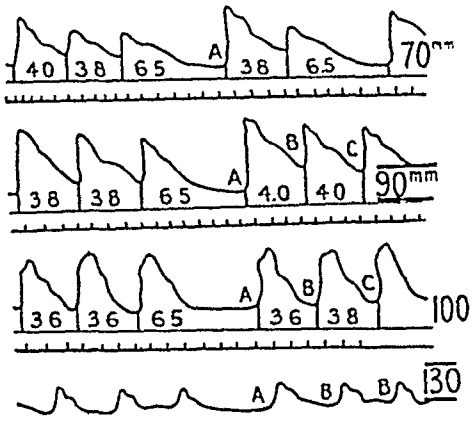
Brachial pulse tracings from another individual with a mild grade of arteriosclerosis, taken at 50 and 90 (diastolic pressure) and 105 and 130 mm. Hg (systolic pressure) respectively, showing an anacrotic wave on the tracings taken at pressure of 105 mm. Hg, not at other pressures. This may explain some false tracings of pulsus tardus obtained with radial sphygmographs.

sphygmographs, when there is no fine regulation of pressure on the artery. Fig. 3 shows that what may appear to be an irregularity in force, when taken below the diastolic pressure, may really be only an irregularity in rhythm, with a fall in pressure, during the long diastoles, for in the tracings taken at pressures above the minimal the apparently weak beats, *B* and *C*, are seen to be as strong as *A*. This is contrasted sharply with the true irregularity

in force and rhythm occurring in the same patient at another time (Fig. 4).*

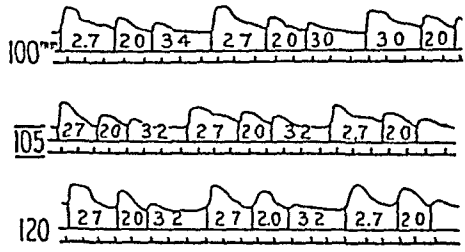
The brachial pulse tracing is very easily obtained, and affords a very convenient standard of time upon which to compare the events

FIG. 3



Brachial pulse tracings from a patient with an irregular pulse. Tracings taken at 70 and 90 mm. Hg (diastolic pressure) show one large beat, *A*, followed by two small ones, *B* and *C*. 90 mm. represent the diastolic pressure after the long pause at *A*. Tracings at 100 mm. Hg, (diastolic pressure in the shorter pauses, *B* and *C*) and tracings at pressures above this show that these latter beats are of force equal to beat, *A*. Hence irregularity in rhythm only.

FIG. 4



Brachial pulse tracings from same patient as in Fig. 3, taken at another time at pressures o 100, 105 (diastolic pressure), and 120 mm. Hg. Irregularity here persists at higher pressures. Inequality in force and rhythm is shown.

in different tracings with one another, by measuring off the time of their occurrence before or after the upstroke in the brachial.† The carotid pulse is taken by applying the receiving tambour

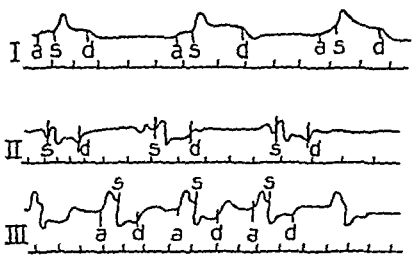
* The same result might be obtained by determining the presence of weaker systoles by the method of Hensen with the Riva-Rocci apparatus (and broad cuff). Raise the pressure in the cuff on one arm, count the pulse rate simultaneously in both—and determine the pressures at which the individual beats appear. If the systolic pressures are equal, and there is irregularity in size in the sphygmogram this is due to irregularity in diastolic pressure.

† The best method for measuring out time relations upon two simultaneously recorded curves is not by exactly superposing the levers, and then dropping a perpendicular from one to the other, but by measuring horizontally the distance of the desired point from the starting point of the curve, and then marking off on the other curve the same distance from the starting point. Small but very important inaccuracies in measurement, as well as much trouble in the adjustment of levers, is thereby obviated.

or funnel, with firm pressure, above and in front of the sternocleidomastoid; for the jugular pulsation, it is applied lightly over the base of the relaxed sternocleidomastoid or over the external jugular vein in the supraclavicular fossa where the vein can be seen to pulsate. The apex tracing should be taken with the receiver as far to the left as possible, for otherwise the curve from the right ventricle is obtained with systolic retraction instead of systolic impulse as shown in Fig. 5.

Type I shows the apex tracing; II is the tracing over the right ventricle with a systolic retraction *s-d*, instead of a systolic impulse; III shows the mixed type, impulse due to the auricle *a-s*, with retraction due to the ventricular systole *s-d*. The systolic retrac-

FIG. 5



Three types of apex tracings: (I) normal apex tracing taken over the left ventricle, showing systolic impulse; (II) from the same person taken over the right ventricle at a point 2 cm medial to (I), showing systolic retraction; and (III) from another patient, showing presystolic impulse *a—s* due to auricular contraction, and systolic retraction *s—d* (the apex beat being due mainly to the right ventricle). For lettering, see Fig. 6.

tion at the apex, so frequently seen in large hearts, is due to the fact that this area is occupied by the right ventricle.

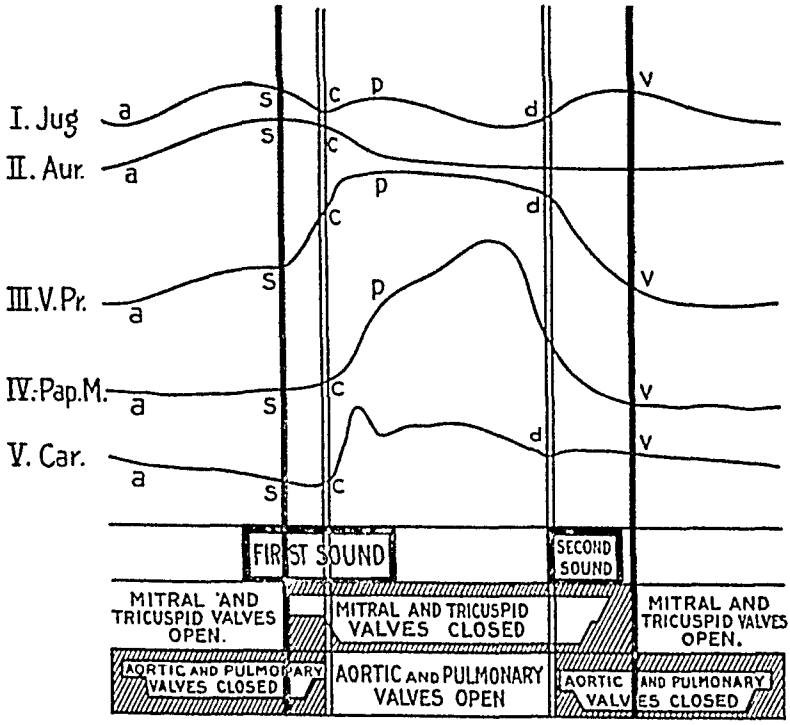
The sequence of events in the heart and great veins is shown in the diagram (Fig. 6), which is a diagrammatic but fairly accurate compilation of the experimental results of Marey,[11] Roy and Adami,[12] Hüethle,[13] Porter,[14] and Einthoven and Geluk.[12] It corresponds with experimental data somewhat more closely than does the diagram of von Frey, which is so frequently figured in the text-books, among others by Mackenzie (*loc. cit.*).*

The curve in Fig. 6 shows a wave *a-s* lasting normally one-sixth of a second, due to auricular systole. This is present upon the

* The time of occurrence of the first sound is still in dispute. The curves of Einthoven and Geluk with the capillary electrometer do not show definitely any sound wave occurring before ventricular systole. On the other hand, those of Huethle (Ueber mechanische Registrirung der Herztöne. Archiv f. d. gesammte Physiologie, 1895, Band lx, S. 263), made with a different recording apparatus, show a definite presystolic sound wave in some but not in all of the cases examined. Moreover, in many cases of heart-block a feeble sound corresponding to the systole of the auricles can be heard over the heart; so that it is probable that in many, though perhaps not in all cases, the first sound begins before ventricular systole, and is produced by vibrations from (1) the contracting auricles, (2) the vibrating valves, and (3) the contracting ventricular muscle.

jugular tracing and also upon most good apex tracings (when taken with the receiver described—but not when the Marey cardiograph tambour is used), and the duration *a-s* marks the period of conduction from auricle to venticle. Then there is the short almost negligible period *s-c* (0.03 to 0.07 second) before the opening of the aortic valves; then a wave *c-p* on the venous tracing just following the rise of pressure in the ventricle, when after closing the mitral and tricuspid valves at *s* the rise of pressure in the ventricles forces these valves back upward into the auricles and causes stasis in the veins. Then comes the fall *p-d* lasting through almost the entire duration

FIG. 6



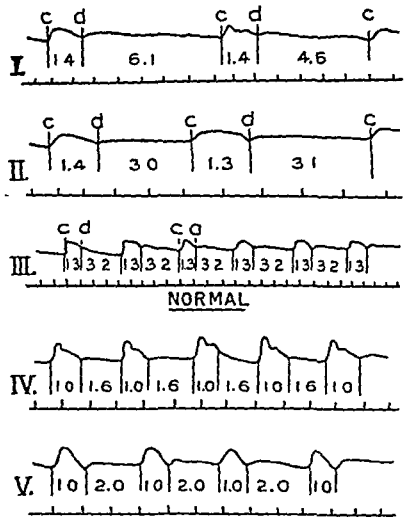
Semidiagrammatic representation of the events in the cardiac cycle: *Jug.*, pulse in the jugular vein; *Aur.*, contraction of the auricle; *V. Pr.*, intraventricular pressure; *Pap. M.*, contraction of the papillary muscles; *Car.*, carotid pulse. Below are given the times of occurrence of the heart sounds and of the opening and the closing of the heart valves.

of the ventricular systole, while the papillary muscles are drawing these valves down again into the ventricle (as shown in Curve 4); this action is further supplemented by the tug upon the great veins directly. At *d*, the instant of the dicrotic notch in the aorta, and practically also in the carotid, systole ceases; and the aortic valves close.

It may be noted in this connection that the duration of the ventricular systole is most accurately measured upon the carotid tracing, for the curve obtained over the apex is rarely definite enough to be relied on. The period of systolic outflow can always be measured,

on the carotid curve, from the beginning of the rise *c* to the dicrotic notch *d*, marking the time during which the aortic valves are open. This has no relation at all to the time from the rise to the first fall in the carotid, as is shown in the tracings. The series of tracings in Fig. 7 shows that in bradycardia the period of systolic output

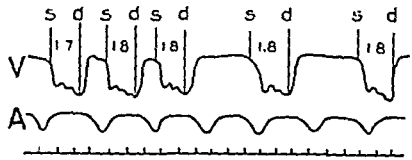
FIG. 7



Carotid pulse tracings, showing periods of systolic output *c—d*, time in fifths of a second: (I) from case of bradycardia; (II) from case of mitral stenosis with snapping first sound, pulse rate 68 per minute; (III) normal individual, pulse rate 64; (IV) case of embryocardia, pulse rate 115; (V) case of febrile tachycardia, pulse rate 100, dicrotic.

(0.28 second) is longer than in tachycardia (0.2 second). Tracings 2 and 4 are from cases with short and sharp first sounds, No. 2 having a normal and No. 3 a shortened period of systolic output. Huethle[16] and Reid Hunt[17] have shown that the immediate result of

FIG 8



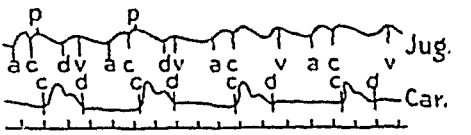
Tracing from the heart of a dog with partial heart-block; occasional failure of the ventricle to respond to one beat of the auricle, showing the duration of the ventricular systole *s—d* unaffected by either the prolonged diastole or the overfilling of the heart after two auricular beats; *V*, ventricular contraction; *A*, auricular contraction.

vagus stimulation is lengthening of diastole without change in duration of systole, whereas accelerator stimulation shortens both in about the same ratio. After prolonged accelerator stimulation or continued loss of vagus tone both systole and diastole are shortened.

The nervous mechanism involved can, therefore, be ascertained only at the immediate onset of a tachycardia, not after it has persisted. Neither extreme prolongation of diastole, nor extreme overdistention of the ventricles, such as is seen in partial or complete heart-block, has any effect whatever upon the duration of ventricular systole (Fig. 8), so that Huethle's statement (*loc. cit.*) that the duration of systole depends upon the amount of blood in the ventricles is not absolutely true.

To return to the diagram (Fig. 6), the next event shown upon Curve I of the jugular pulse is a very important one for the interpretation of pulse tracings: a rise *d-v* beginning a little before the closing of the aortic valves at *d* and lasting exactly to the opening of the tricuspid valves at *v*. It is due to the fact that the papillary

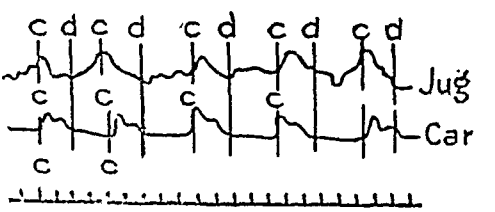
FIG. 9



Normal or physiological venous pulse from the jugular vein, *Jug.*, and pulse from the carotid artery, *Car.* Lettering as in Fig. 6.

muscles and the heart as a whole have ceased to pump blood out of the veins into the auricles, and the blood accumulates until it is let out into the ventricles by the opening of the tricuspid valves. After this fall there are no further waves upon the jugular tracing until the next auricular wave. If any other wave appears it is abnormal, and is to be interpreted by referring it to the various events that appear normally.

FIG. 10



Normal or physiological venous pulse from the jugular vein, *Jug.*, and pulse from the carotid artery, *Car.* Type considered normal by Sahli. Lettering as in Fig. 6.

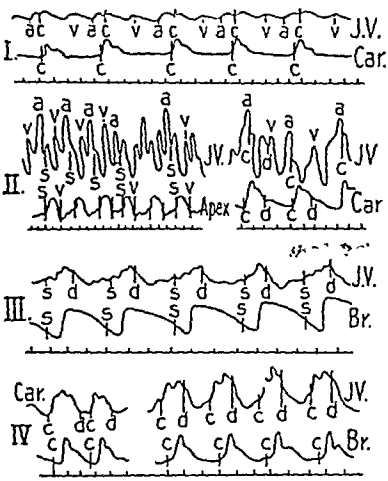
Fig. 9 shows the normal jugular tracing in which can be seen all the events shown in the diagram for the jugular vein—the auricular wave *a-c;* the rise followed by the collapse during ventricular systole *c-p-d;* the stagnation wave terminating with the opening of the tricuspid valve *v*. The presystolic filling due to auricular systole *a-c* is shown on almost all normal individuals if the veins are full enough to give any pulsation at all. Sahli and Riegel give

as normal a second type in which the auricular wave *a-c* is absent; this is shown in Fig. 10, but the first type is much more frequent.*

Moreover, there are very many cases in which no tracing at all can be obtained from the veins. These may be divided into two classes: (1) Those in which the veins are not full enough to give visible pulsation, and (2) cases of phlebosclerosis in which the walls of the vessels are too rigid to respond to the small changes of pressure, or in which the valves of the veins damp the pulsation completely.

We shall now consider the pathological forms of venous pulse: First, the transiton from normal to tricuspid insufficiency, Fig.11.

FIG 11



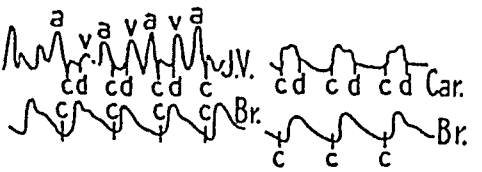
Transition from the normal jugular venous pulse, *J. V.*: (I) to the venous pulse of tricuspid insufficiency (IV); (II) veins full and all waves accentuated, but no abnormal waves present; (III) gradual filling of veins during systole, with diastolic collapse, from same case as IV, but two weeks earlier; *s—d* ventricular systole; *Br.*, brachial pulse at diastolic pressure.

Curve I shows a normal venous tracing. Curve II is at first glance of entirely different form, but on analysis is seen to be exactly the same only with accentuation of each wave, on account of the overfilling of the veins. In curve III the auricular presystolic wave does not appear at all, and during systole there is a gradual systolic filling instead of systolic collapse. This is due to the fact that the auricle is already overfilled, no more blood can be pumped into it and out of the veins, hence they continue to fill gradually until the tricuspid valves open and the diastolic collapse takes place, as noted

* Jugular tracings of this type seen with weak hearts are sometimes mistaken for manifestations of tricuspid insufficiency, but the presence of the *systolic fall p-d* instead of the systolic plateau (Fig. 2, Curve 4) allows them to be distinguished. The absence of the auricular wave *a-c* may be due to a weak right auricle or to conditions within the heart (abnormal relaxation of ventricles in diastole, etc.) facilitating the flow from auricle to ventricle; or, on the other hand, the pulse may be simply communicated from the carotid artery.

by Gerhardt.[18] Curve IV represents the same case at a later stage when tricuspid insufficiency is already definite; the curve in the veins (the so-called ventricular type of venous pulse) exactly records the intraventricular pressure with sudden systolic filling and diastolic emptying. On these tracings the auricular presystolic wave does not appear, probably because the auricle is contracting too feebly, although still strongly enough to stimulate the auriculoventricular bundle, and thereby the ventricle. Experimentally one often sees these very feebly contracting overdistended auricles in failing hearts of dogs. Sometimes there is even complete paralysis, first mentioned by v. Frey and Krehl,[19] but in such cases the auricle may resume action after a period of rest. James Mackenzie[20] and Wenckebach[21] think that in all such cases the ventricle contracts before the auricle, basing their opinion upon the experimental work of Lohman[21] done in another connection. However, there is no evidence at all conclusive that such is the case in man, and in failing hearts of animals this reversal of rhythm is never seen. On the contrary, the period of auriculoventricular conduction is lengthened rather than shortened as the heart weakens. The venous pulse, then, gives

FIG. 12



From a patient with aortic insufficiency, œdema, dyspnœa of cardiac origin, and enlarged (non-pulsating) liver. Nevertheless, a normal tracing from the jugular vein (*J. V.*), showing all the physiological waves and absence of tricuspid insufficiency.

the most definite diagnostic sign of tricuspid insufficiency, for with every tricuspid insufficiency we have marked systolic filling of the veins instead of systolic collapse, and only one venous pulsation with each carotid beat instead of two as normally. The two pulsations seen normally are the systolic fall (*p-d*) and the fall after the stagnation wave *v*. That cardiac œdema and dyspnœa with distention of the peripheral veins may persist for days without any insufficiency of the tricuspid valve is shown by the tracing (Fig. 12) taken from a case of aortic insufficiency in which these signs and symptoms were present, but in which there was no back-flow into the veins during ventricular systole. Mackenzie[20] has also given a tracing from such a case.

Another tracing which affords evidence of tricuspid insufficiency is the tracing from the liver. Normally, as the liver rests upon the diaphragm just beneath the right ventricle, it is pushed down as the ventricle fills in diastole, and pushed up by the abdominal organs when the ventricle draws up in systole,—in other words, there is systolic retraction of the liver. But when there is tricuspid insuffi-

ciency the blood is forced back into the liver during systole, and a systolic impulse is given instead, a fact noted by Kreysig in 1814 (*loc. cit.*) and by Mahot in 1869.[22] Fig. 13 shows the two types mentioned.

We may next consider briefly the irregularities of the heart, which may be divided into several groups.

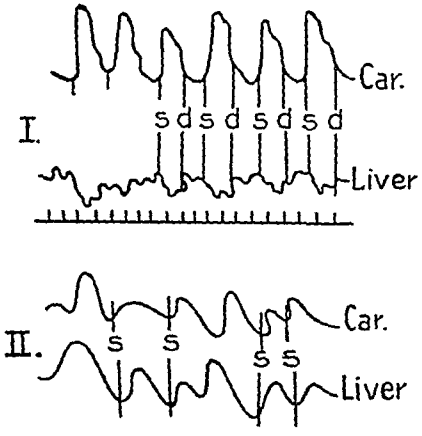
1. Those arising from intermittent action of the spinal and medullary centres especially through the vagus.

2. Irregularities arising at the mouth of the vena cava and in the auricle, due to disturbed contractility or overdistention of the auricle, with auricular extrasystoles.

3. Irregularities due to premature contractions of the ventricle, arising in the ventricle from similar causes.

4. Irregularities due to failure of the auriculoventricular bundle to conduct, so that the ventricle does not respond to all the auricular beats, the so-called partial or complete heart-block.

FIG. 13

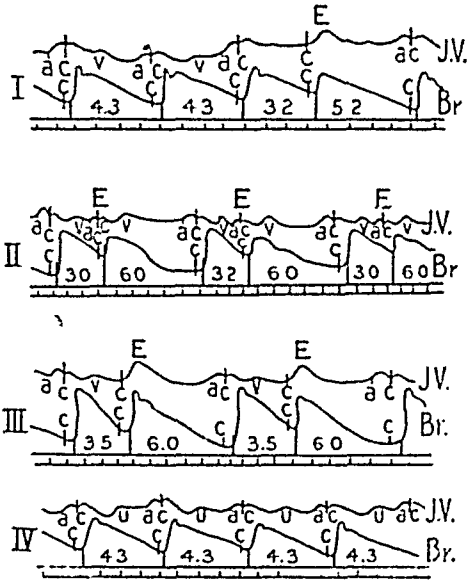


Two types of pulsation over the liver: (I), normal with systolic retraction of the liver *s–d*; (II) from case of tricuspid insufficiency, systolic protrusion of liver.

5. There may be, as now claimed by Mackenzie and Wenckebach (*loc. cit.*) and some others, a fifth form of extreme tachycardia due to spontaneous initiation of the cardiac rhythm by the rhythmic contraction of the auriculoventricular bundle of His, auricles and ventricles taking up the rhythm and contracting simultaneously. It may be said, however, that the experimental and clinical evidence for this theory may be explained in other ways. In stimulating the auriculoventricular bundle electrically the simultaneous contractions of auricles and ventricles obtained by Lohmann may have been due to escape of electrical stimulus to these parts directly (as suggested by Dr. Erlanger). On the other hand the absence of an auricular wave on venous tracings may be due to weakly contracting auricles.

Clinically, it is not especially difficult to differentiate between irregularities arising in the ventricle and those arising in the auricle. Cushny and Matthews[23] have shown that if the ventricle is stimulated by an induction shock an early contraction follows the stimulation; the ventricle then fails to respond to the next regular stimulus coming down from the auricle, so that this impulse is skipped and the regular rhythm is resumed when the ventricle responds to the second regular impulse (Fig. 14, Curve II), that interval, occupied by the regular systole and the premature systole until the next regular systole, is exactly twice the interval between two beats, as shown on the tracing (Fig. 14, Curve IV). Further, it can be seen

FIG. 14



Irregularities of the heart: (I) showing a ventricular extrasystole *E*; (II) auricular extrasystoles at *E*, *E*, *E*; (*J. V.*), jugular pulse. *Br.*, brachial time in $\frac{1}{5}$ second; (III) continuous bigeminal pulse due to ventricular extrasystoles; (IV) same one hour after atropine, $\frac{1}{120}$ grain, showing regular pulse and change in the venous pulse.

that the extrasystole is not preceded by an auricular wave as are other systoles, but the auricle when it contracts at all does so after the ventricle and during the period of ventricular contraction, giving rise to the large wave (Fig. 14, Curve I, *E*). These two points—absence of the auricular wave on the venous tracing, and duration of the regular systole plus extrasystole always equal to twice the interval between two regular beats, characterizes the extrasystole of ventricular origin.

Cushny and Matthews (*loc. cit.*) further showed that when the auricle was stimulated by a single induction shock, the regular con-

* Clinically, the ventricular origin of the extrasystole may sometimes be noted from the fact that although corresponding to each regular systole there are two pulsations seen in the jugular vein, corresponding to the ventricular extrasystole there is but one (see Fig. 14), whereas with the auricular extrasystole both waves are still seen.

traction and the extra contraction following occupy less than twice the regular period (This shortening of the compensatory pause to less than the interval between two regular beats does not invariably occur, but when present is characteristic of auricular extrasystoles). Here, of course, the venous pulse still shows the auricular wave (Fig. 14, Curve II, *E, E, E*) for extrasystole as well as for regular systole. These two points characterize the extrasystole of auricular origin. Of course, just as one extra stimulus is sent prematurely, several extra impulses in succession may reach either auricle or ventricle. When this occurs a series of extrasystoles are seen, and two, three, or four, etc., times the regular interval between pulse-beats elapses from the beginning of the last regular beat before the extrasystoles to the beginning of the first regular beat following them.

In the case of all extrasystoles, the earlier the occurrence the shorter and weaker the contraction, for the heart has then not fully recovered from the preceding contraction. If the systole occur too early it may be so weak that the intraventricular pressure never reaches the minimal pressure in the aorta, the aortic valves are not opened, and a beat is felt at the apex which does not reach the arteries at all, the so-called "frustrane contractionen" of Hochhaus and Quincke.[24] The heart recovers more quickly after an incomplete systole than after a large contraction.

To return to the type irregularities: besides the irregularity from extrasystoles arising in the auricles and in the ventricles, there is the purely neurogenic type of irregularity, in which the regular rhythm is interrupted by a long pause, usually less than twice the pulse interval (Fig. 3). This is what Mackenzie calls the youthful type, because it is very common in otherwise healthy children and young adults. Reyfisch[25] has recently shown that this is due to occasional overaction of the vagus, because in these cases the pulse becomes absolutely regular after giving $\frac{1}{120}$ to $\frac{1}{60}$ grain of atropine to paralyze vagus action. In these cases we sometimes have, as shown in Fig. 3, irregularity in rhythm without irregularity in force.

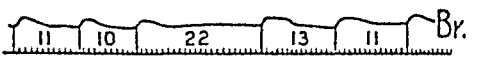
Long ago Dehio[26] was able to show that atropine made some pulses regular and had no effect at all on others, and although his work was done before the Engelmann doctrine of extrasystoles, in the light of the newer work, this enables us to differentiate between the three forms of irregularity—the neurogenic which becomes regular under atropine by removing the irregular stimuli, the auricular irregularity due to disturbed contractility and rhythmicity of the auricle which will not become regular after atropine, and the ventricular extrasystole. In the latter case as shown by Dehio, but first interpreted by H. E Hering,[27] the rate of the auricles becomes accelerated after paralysis of the vagus, and when they are beating fast enough the stimuli from the auricles reach the ventricles before the extra stimuli, and the pulse becomes regular, each ventricular contraction being preceded by an auricular contraction

(Fig. 14, Curves III and IV). The atropine test combined with the venous pulse tracing allows us, therefore, to differentiate between the true cardiac neurosis and the myogenic disturbance of contraction.

The fourth type of irregularity is the type of heart-block, partial or complete, in which the ventricle either occasionally fails to respond to some of the impulses from the auricle or beats absolutely independently of it. The subject of complete block has been very completely discussed by Dr. Erlanger.[25]

Cases of partial block are probably not infrequently seen after fevers, especially as shown by Mackenzie (*loc. cit.*) in the post-influenzal bradycardias, in which he has found the ventricle failing to respond to alternate auricular impulses.*

FIG. 15



Brachial pulse from case of severe pneumonia, showing an occasional omission of a beat. Time marked by vibrating spring at the rate of about 20 per second.

Mackenzie also states that in the fatal pneumonias there is a dropped" beat with exactly twice the normal interval, which in his experience is always a herald of death. But in one case under my care, in San Francisco, recovery followed in spite of the dropped beat (Fig. 15). (No sounds could be heard over the heart during the long pause.) So far as I know there are no venous pulse records of such cases, but they are probably instances of partial heart-block. Stähelin[28] has observed what may be similar beats in convalescents from pneumonia after exercise, and it is not improbable that post-febrile syncopes, and perhaps the sudden deaths after diphtheria, may be due to a Stokes-Adams syndrome from toxic heart-block.

* Such failure of the ventricle to respond to alternate beats of the auricle might be due to either of two causes:

1. There may be a slight organic lesion of the myocardium or endocardium in the vicinity of the auriculoventricular bundle just sufficing to produce this mild grade of heart-block. Erlanger and Hirschfelder[29] have shown that in experimental partial heart-block in dogs, brought about by slightly clamping the auriculoventricular bundle so that the ventricles respond to only alternate contractions of the auricles, stimulation of the vagus improves the conductivity and brings about response to each auricular contraction.

2 Bayliss and Harling,[31] Reid Hunt, l. c., and others have produced a similar dropping o alternate beats by the ventricle upon careful stimulation of the vagus and in some cases upon increasing the tone of the vagus. Rihl (Zeitschrift f. experimentelle Pathologie und Therapie, Berlin, 1905. Band ii, S. 83) has shown that in some clinical cases where the ventricle responds to alternate beats of the auricle response to each beat occurs after atropine is given, and on the other hand that dropping of beats of the ventricle can be brought on in normal individuals by forcible pressure on the vagus in the neck.

Hence it seems possible to differentiate between these two groups of partial heart-block by the atropine test—the dropping of beats disappearing after atropine when the disturbance is functional; the dropped beats continuing after atropine when there is an organic lesion near the auriculoventricular bundle.

These are some of the questions for subsequent investigation, but enough has been done to establish the method of multiple tracings as a routine in the clinical study of heart diseases.

Unfortunately, the excellent series of papers of H. E. Hering, J. Rihl and O. Pan in the *Zeitschrift f. experimentelle Pathologie and Therapie*, 1905, Band i und ii, came to hand after this article had been prepared for the press; all who are interested in the subject will certainly consult them in the original.

BIBLIOGRAPHY.

1. Homberg. Sur un battement de veines semblables au battement des artères, Hist. Acad. roy. d. sc. (de Paris), 1704, Amst., 1707, 218–223. C. Zuliani, De quibusdam cordis affectionibus, Brix, 1805. C. Benson, Case of Pulsation in the Veins of the Upper Extremities, Dublin Journal of Med. and Chem. Sci., 1835–6, viii, 324–332. F. L. Kreysig, Die Krankheiten des Herzens, Berlin, 1814 and 1815, cited from Friedreich.

2. Barry. Experimental Researches on the Influence of Atmospherical Pressure upon the Blood in the Veins. G. Wedemeyer, Untersuchungen ueber der Kreislauf des Bluts und insbesondere ueber die Bewegung desselben in den Arterien und Capillargefaessen, 8°, Hannover, 1828.

3. Weyrich. De cordis aspiratione experimenta, Dorpati, 1853; cited from E. Gottwalt, Der Normale Venenpuls, Arch. f. d. ges. Physiol., Bonn, xxv.

4. H. Bamberger. Beobachtungen ueber den Venenpuls, Wurzb. med. Ztschr., 1863, iv, 232–248.

5. N. Friedreich. Ueber den Venenpuls, Deutsches Arch. f. klin. Med., Leipz., 1865-6, i, 241–291, 2 pl.

6. T. Engelmann. Ueber die Leitung der Bewegungsreize im Herzen, Arch. f. d. ges. Physiol., Bonn, 1894, lvi, 149–202, 2 ch. Ueber den Einfluss der Systole auf die motorische Leitung in der Herzkammer, mit Bemerkungen zur Theorie allorrythmischer Herzstoerungen, Onderzoek ged. in h. physiol, Lab. d. Utrecht, Hoogesch., 1896, 4, R., iv, 74–106, 2 pl.

7. H. E. Hering. Ueber die gegenseitige Abhängigkeit der Reizbarkeit, der Contractilitaet, und des Leitungsvermoegens der Herzmuskelfasern, Arch. f. d. ges. Physiol., Bonn, 1901, lxxxvi, 533.

8. K. F. Wenckebach. Zur Analyse des unregelmässigen Pulses, Ztschr. f. klin. Med., Berl., 1898, xxxvi, 181–199, 1 diag.; 1899, xxxvii, 475–488, 1 pl.

9. J. Mackenzie. The Study of the Pulse and Movements of the Heart. London, Macmillan, 1903. The Venous and Liver Pulses, and the Arrhythmic Contraction of the Cardiac Cavities, Journ. Path. and Bacteriol., Edinburgh and London, 1893–94, ii, 84, 273.

10. J. Erlanger. A New Instrument for Determining the Minimum and Maximum Blood Pressures in Man, Johns Hopkins Hosp. Rep., Balt., 1904, xii, 53.

11. E. J. Marey. La circulation du sang a l'état physiologique et dans les maladies, 8°, Paris, 1881.

12. C. S. Roy and J. G. Adami. Heart-beat and Pulse-wave, Practitioner, Lond., 1890, xliv, 81, 161, 241, 347, 412; xlv, 20.

13. K. Huethle. Beiträge zur Haemodynamik, Arch. f. d. ges. physiol., Bonn, 1891, xlix, 29–104, 1 pl.; ibid., 1895, lx, 263–290, 1 diag.

14. W. T. Porter. Researches on the Filling of the Heart, J. Physiol., Cambridge, 1892, xiii, 513–553, 2 pl.

15. W. Einthoven and M. A. J. Geluk. Die Registrirung der Herztoene, Arch. f. d. ges. Physiol., Bonn, 1894, lvii, 617–639.

16. K. Huethle. Beitrage zur Haemodynamik, ibid., 1891, xlix, 29–104, 1 pl.

17. R. Hunt. Direct and Reflex Acceleration of the Mammalian Heart, Amer. Journ. Physiol., 1899, ii, 395.

18. D. Gerhardt. Die diagnostische Bedeutung des diastolischen Venencollaps, Ztschr. f. klin. Med., Band xxxiv, 353. Einige Beobachtungen an Venenpulsen, Arch. f. exper. Pathol. und Pharmakol., 1902, xlvii, 250.

19. M. v. Frey and L. Krehl. Untersuchungen ueber den Puls, Arch. f. Physiol., Leipz., 1890, 31.

20. J. Mackenzie. Observations on the Inception of the Rhythm of the Heart by the Ventricle as the Cause of Continuous Irregularity of the Heart, Brit. Med. Journ., Lond., 1904.

i, 529-536. New Methods of Studying the Affections of the Heart., ibid., 1905, i, 519, 587, 702, 759, 812.

21. J. Mackenzie and K. Wenckebach. Arch. f. Physiol., Leipz., 1905. Lohmann, Zur Automatie der Brückenfasern des Herzens, Arch. f. Physiol., Leipz., 1904, Suppl. Band, 265-270.

22. Mahot. Des battements du foie dans l'insuffisance tricuspide, Thèse, Paris, 1869.

23. A. R. Cushny and S. A. Matthews. On the Effects of Electrical Stimulation of the Mammalian Heart, Journ. Physiol., Cambridge, 1897, xxi, 214-230.

24. Quincke and J. Hochhaus. Ueber frustrane Herzcontractionen, Deutsches Arch. f. klin. Med., Leipz., 1894, liii, 414.

25. Reyfisch. Klinische und experimentelle Erfahrungen ueber Reizungen des Herzvagus, Berl. klin. Wchnschr., 1905, 1468.

26. K. Dehio. Ueber den Einfluss des Atropins auf die arhythmische Herzhätigkeit, Deutsches Arch. f. klin. Med., Leipz., 1893, lii, 97.

27. H. E. Hering. Ueber continuierliche Herzbigeminie, Deutsches Arch. f. klin. Med., Leipz., 1904, lxxix, 175-193, 1 pl.

28. J. Erlanger. A Report of Some Observations on Heart-block in Mammals, Johns Hopkins Hosp. Bull., Balt., 1905, xvi, 234. Heart-block in Mammals, with Especial Reference to Stokes-Adams Disease. Journ. Exper. Med., N. Y., 1905, vii, 676. An Instance of Complete Heart-block in Man, Proc. Am. Physiol. Soc., Boston., 1904-5, p. xxvi.

29. J. Erlanger and A. Hirschfelder. Vorläufige Mittheilung ueber die Physiologie des Herzblocks in Säugetieren, Zentralbl. f. Physiol., Leipz. u. Wien., 1905-6, xix, 9-12. Also Further Studies on the Physiology of Heart-block in Mammals, American Journal of Physiology, vol. xv, p. 153, 1906.

30. Stachelin. Ueber den Einfluss des Muskelarbeit auf die Herzthätigkeit, Deutsches Arch. f. klin. Med., Leipz., 1900, lxvii, 147.

31. W. M. Bayliss and E. H. Starling. On Some Points in the Innervation of the Mammalian Heart, Journ. Physiol., Cambridge., 1892, xiii, 407.

INSUFFICIENCY OF THE TRICUSPID VALVE IN THE COURSE OF PERNICIOUS ANEMIA.[1]

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The influence which anemia, of whatever type or cause, exercises over the nutrition and consequently the function of the heart muscle has been the source of frequent discussion. The effects which these changes have upon the size, shape, rhythm, and tone of the heart have been extensively considered. Particularly is this true of the so-called relative insufficiency of the mitral valve. It would be quite aside from the subject which I wish to present briefly to enter into any discussion of the mechanism of these insufficiencies. Whether they are due to dilatation of the auriculoventricular orifice or, as is more likely, to inco-ordinate action of the papillary muscles, has no bearing on the question of their existence. While the differentiation of this type of insufficiency from the accidental heart murmurs so common in anemia is difficult and often impossible, yet after making due and sufficient allowance for error, the cases of

[1] Read at a meeting of the Association of American Physicians, Washington, D. C., May 15 and 16, 1906.

leakage through the mitral valve in the course of anemia are not at all uncommon.

While the existence of this type of mitral insufficiency has been generally recognized for years there has, curiously enough, been little or no consideration of the possibility of the same thing happening in the right ventricle. This is the more striking because one might expect the thin walls of the right ventricle to yield more readily than those of the left, and while the diagnosis of the relative mitral insufficiency is surrounded by great difficulties and uncertainties, the tricuspid insufficiency can be diagnosed with certainty and usually with ease.

I am inclined to believe that the same thing is true of these relative insufficiencies as has been true of so many things, namely, that they are common enough, but are entirely overlooked until attention is forced to them by some particularly striking example, and the attention, once aroused, finds them common.

The first case, which I wish to report, was too striking to permit of its being overlooked. The subject was a lady of seventy-odd years, whom I saw with Dr. Hutchison, of Chicago. She had been gradually failing for some months, but as the loss of strength was slow and unaccompanied by pain or any striking symptom, nothing was done for a long time. Dr. Hutchison had been caring for her for some weeks, having made a diagnosis of primary pernicious anemia—a diagnosis in which I fully agreed. The thing which particularly struck me about the patient was the intensity and character of the pulsation in the external jugular veins. These veins were greatly distended, so much so that they could be easily taken between the fingers, and on timing the pulsation it was found to be systolic, corresponding exactly with the apex beat. The pulse in the jugulars was markedly stronger than the pulse in the carotids. The heart was found to be but slightly enlarged to the right, the absolute dulness being at the right border of the sternum; the second pulmonic tone was of approximately normal intensity. There was a systolic murmur, loudest at the apex. The liver was only slightly enlarged and did not pulsate. There was no œdema of the legs, no dyspnœa, and no cyanosis. She could sleep without having the head elevated.

An unfavorable prognosis was made, largely because it seemed likely that a pernicious anemia which had caused such alteration in the heart nutrition that a tricuspid insufficiency resulted, would probably end fatally in a short time. This did indeed happen, death taking place little more than a week later.

This was the first instance of this which I had seen, but curiously enough, six days later I saw another. The second patient, also a woman, was younger, fifty-three years. She had been seriously ill three years previously with an anemia which had been called pernicious. The woman at that time became so low that her life was

despaired of, but she finally improved sufficiently to resume her household duties and enjoy good health.

Three months before I saw her she began to fail, and not improving under the treatment which three years before was successful, I was asked to see her. When I saw her she was lying unconscious, having been in this condition for about three hours. She was profoundly anemic, lemon-yellow in color, and moderately emaciated. Like the first patient, she showed a very active positive venous pulse in the jugular veins. This pulsation could also be seen and felt in the small veins on the anterior surface of the chest and upper arm. The heart was only moderately dilated, with a pulse of 130. The second pulmonary sound was not reduced in intensity. The systolic murmur which could be easily heard was no louder over the auscultation point of the tricuspid than elsewhere. The liver was not enlarged and there was only slight œdema of the legs. The blood gave the usual picture of pernicious anæmia, but as the patient died some three hours later only one examination could be made.

The third patient is an Irish carriage painter, of forty years, whom I saw in Dr. Slaymaker's service at the County Hospital in Chicago. This patient first entered the hospital in the fall of 1903 complaining of girdle sensation, numbness and tingling in the legs and arms, and ataxia, especially marked in the legs. He was in the hospital for some months, but left improved. He continued at his work at intervals and re-entered the hospital in March of this year. Examination shows a tall, slender, emaciated man, lemon-yellow in color. The apex of the heart is in the fourth interspace in the nipple line, the absolute dulness is at the right border of the sternum, to the upper border of the third rib, and to the apex-beat. The relative dulness reaches one and one-half inches to the right of the right border of the sternum. The second pulmonary tone is accentuated; there is a loud systolic murmur, loudest at the third left interspace. The external jugulars show a positive, systolic centrifugal pulsation. The liver is not enlarged, there is no œdema, cyanosis, or dyspnœa. The blood shows the ordinary picture of pernicious anemia.

We have then three cases of pernicious anemia accompanied by a positive, systolic centrifugal pulse in the external jugular veins. Two of the cases ended promptly in death; the third patient is still alive and is improving somewhat.

There are several ways in which these cases differ from the ordinary form of relative tricuspid insufficiency. As seen so frequently, this lesion is due to dilatation of the right heart, because of the excessive work thrown upon it by a mitral lesion, usually a combined stenosis and insufficiency, or by a gradually progressive emphysema of the lungs or some other pulmonary process interfering with the passage of the blood from the right to the left heart. In addition to these one sees less often cardiac dilatation and consequent tricuspid leakage from acute or more often chronic

myocarditis, and still less often the same thing happens in the course of aortic lesions. In all of these instances the tricuspid insufficiency is accompanied by marked cyanosis, dyspnœa, passive congestion of the liver, œdema of the legs and often of the body cavities. All of these phenomena were conspicuously absent in the cases reported. In addition to these differences, stress should be laid on the fact that while all of the cases reported showed some enlargement of the heart, in no instance did it compare in degree with that seen in the commoner instances of this lesion

Shortly after the first two cases were seen, I read an article by Leube,[1] who reported seven cases of relative tricuspid insufficiency in the course of chlorosis. He points out the same clinical differences which struck me. Among the cases, which he reports were three which presented the positive venous pulse without there being any other physical signs of tricuspid insufficiency. One of these did so later and Leube expresses the opinion that all were cases of leakage through this valve, although in some instances the leak is so slight as to cause no other physical signs. He lays much stress upon the presence of systolic murmurs over the auscultation area of the tricuspid, as an important physical sign of this lesion. Such a murmur was not present in any of my three personal observations, and I may say that I have only rarely been able to find such a murmur in the common cases of this lesion.

Whether one is warranted in drawing any inferences as to prognosis from the fact that two of the three patients promptly died, cannot yet be decided. That can happen only after an accumulation of data. The fact that I have seen three such cases in the period of six months, would lead to the expectation that data will accumulate rapidly, once attention is drawn to the matter.

Since this report was made to the Association of American Physicians, I have seen a fourth case presenting the same feature:

A farmer, aged forty years, giving a history of a period of weakness and anemia one year ago, was admitted to the hospital complaining of loss of weight, exhaustion, and dyspnœa on exertion. The blood findings were those of pernicious anemia, and examination of the jugular veins showed a positive pulse. The absolute dulness of the heart was enlarged to the right border of the sternum, the second pulmonary sound was of normal intensity, and there was a systolic murmur at the apex. The liver was enlarged downward about one inch, and was not tender or painful. There was no cyanosis or dyspnœa, except on exertion, and no œdema.

[1] Zeitschrift f. klinische Medizin, 1905, lvii, 199.

ELEPHANTIASIS NON-PARASITICA, SECONDARY TO CHRONIC CARDIAC DISEASE AND REPEATED ŒDEMA OF PREGNANCY.

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An early case of enlargement of the lower limbs to a "most monstrous magnitude" from anasarca, and two cases of obliteration of the thoracic duct, probably without enlargement of the limbs, one from Valsalva (1666–1723) and one from Santorini (1681–1736), are referred to by Morgagni.[1] In 1817 Chevalier[2] wrote of a case of elephantiasis of the right leg following an attack of phlegmasia alba dolens, and in the same year Kennedy[3] contributed an article concerning a patient observed in Madras in 1796.

Kennedy's[3] patient was a male Madrasi, thirty-five years old, who had received six wounds of the left arm from a bursting matchlock. The smaller wounds healed in three months and the larger in four months, during which time much pus was discharged and the head of the ulna came away. The history after the first day was that of an infected wound. The heat, pain, and throbbing were relieved by cold applications, but the enormous swelling, which had gradually extended up his arm, never subsided, and when the wounds had healed the left arm was twice the size of the right. The arm was finally amputated.

Wormi[5] reported a case of enlargement of the left arm consisting of distention of the veins, chronic œdema, thickening of the skin and aponeurosis, and no pus, resulting from complete obstruction and dilatation to double its size of the left subclavian vein from pressure by a yellow, hard, slightly adherent mass at the junction of the subclavian with the jugular. A similar mass pressed upon the descending portion and obliterated the outlet of the thoracic duct, and a bony pelvic tumor by pressure caused extensive œdema of the right thigh. Turner[6] in 1859 reported two cases of complete obliteration of the thoracic duct by pressure from an aneurysm of the aorta, in one of which the area of obliteration extended from the second to the fifth dorsal vertebra, in the other it was opposite the level of the eighth dorsal vertebra.

Not until 1863 was the filaria parasite discovered by Demarquay,[7] and not until 1874 were cases of elephantiasis arabum described by Lewis.[8] In 1867 T. Carr Jackson[9] reported an interesting case of elephantiasis following infection, in which the elephantoid swelling of the left thigh followed the occurrence of a large intraperitoneal "abscess" extending transversely across the lower abdomen. Three days after recovery from the abscess the thigh began

to swell and during the succeeding six years the dilated lymph varices over the thigh occasionally ruptured and discharged.

The two excellent monographs by Samuel C. Busey,[10] [11] of New Orleans, published in 1878, included the reports referred to and reports of cases of diseased conditions of the lymph channels observed by himself and published in the *New Orleans Medical and Surgical Journal* during the years from 1876 to 1878 inclusive. Busey's two monographs are classics. In summing up certain cases of non-parasitic elephantiasis Busey[10] concluded that their development depended upon some "congenital defect, from nutritive disturbances and changes taking place during intrauterine life, and some acquired factor such as local inflammation." He mentioned two forms, viz., congenital and acquired. The congenital form, resulting from congenital hypertrophy, occurs in acephalic and other monsters, is local, and affects isolated portions of the body, one or both legs, most frequently the right leg. In later life the immediate cause of enlargement may be an inflammation of the derma involving the bloodvessels and lymphatics or primarily the lymphatics, with effusion; this may result in hypertrophy beginning primarily in the subcutaneous tissue and possibly extending to and involving the other soft tissues (muscles, nerves) and the bony structures. The congenital form is usually of the type elephantiasis mollis of Virchow. The conclusion is inevitable (p. 165) that "blood impoverishment, a meagre diet, and bad hygiene are at least exciting agencies which call into active operation a pre-existing predisposition." . . . "These circumstances relate more especially to certain acquired forms; but a large number of these manifestly originating in some congenital abnormality are developed in after life under influences which may be regarded as exciting causes." The age of puberty is regarded by several writers as the period of most prolific development.

In the acquired forms, such as elephantiasis arabum (filariasis) and the condition due to repeated local inflammation and pressure upon large vessels, the tissue changes correspond to true elephantiasis dura of Virchow. Cholmeley[12] in 1869 reported a case dependent upon "obstructed heart circulation and engorgement of lymph channels in parts remote from the direct influence of such impediments," a condition apparently similar to that of the case here reported. A female child, the fourteenth of seventeen children, the sixteen in good health, was born at term, deeply cyanosed. Repeated attacks of dyspnœa and "inflammation of the chest" occurred during a period of from four to five years. The child was always well nourished and fat, with good, bright color in the cheeks, but easily affected by cold, and at such times complained of want of breath and a feeling of tightness in the chest, and the complexion assumed a markedly livid tint. The pulse was "normal in frequency, rhythm, volume, and force," but all over the heart was heard

a soft blowing systolic murmur loudest at the junction of the second left costal cartilage with the sternum. "During her sixth year swelling appeared over the right ankle, which gradually extended upward, though not above the knee until two years had elapsed; but in the third year when the patient was between seven and eight, the 'swelling extended slowly and steadily upward till her whole limb was implicated,' but has not gone above 'the inguinal line.' The increase in the size of the swelling was always greater toward evening, and did not affect the foot when a boot was put on when the child first got up."

"The entire limb was uniformly enlarged, felt 'soft, firm, and elastic,' the lower part being firmer and more tense than the upper; in color and temperature the limbs did not differ." . . . "The skin was smooth and soft as far down as the middle third of the leg; below it was 'harsh, rough, dry, and scaly; on the outer surface of the ankle were a number of 'soft, smooth, red, flattened papules,' not larger than a split pea. On the hypertrophied skin of the great, second, and third toes were 'rough, hard elevations looking much like a half-aborted and dried herpetic eruption, from which occasionally a discharge took place,' and over the tendo Achillis was a 'humid patch from which a milky looking alkaline fluid dripped,' similar in character to the fluid which issues through punctures made into the lower part of the limb, which exhibited under the microscope broken-up cells, granular matter, some oil globules, blood corpuscles, and 'coagulated on boiling.'"

The comparative measurements of the lower extremities were as follows:

	Left.	Right.
At the ankle	8 inches	9¼ inches
At the midleg	9 inches	14 inches
Below the knees	9¼ inches	14½ inches
Above the knees	10½ inches	16½ inches
Upper part of thighs	15 inches	17½ inches

(Child 7–8 years old)

"There was no fulness or swelling of any kind detected in the groin or pelvis; nothing abnormal in the condition of the right nympha or labium; never any pain in the limb; nor any injury, accident, or known cause to account for the condition." Of Cholmeley's case Busey states (pp. 136–138): No postmortem was permitted so we cannot "positively establish any connection between the lymph stasis, which was first apparent near the ankle, and the disturbed cardiac circulation—the cause of which was probably located in the pulmonary artery; and though it seems improbable that an obstructive force originating in the retardation of the blood current from the right ventricle could be transmitted backward along the fluid contents of the thoracic duct and lymph vessels and glands through which the lymph must pass from the lower extremity to

reach the receptaculum, yet in view of cases previously cited such explanation of the phenomena cannot be excluded."

Localization of stasis to the one extremity "must, perhaps, find its explanation in some abnormal condition of the lymph vessels of the right lower extremity, which like the cardiac defect was probably congenital . . . The early history of the swelling and engorgement shows that the accumulation was hypostatic. Movement of the fluid, according to relative elevation of the upper and lower parts of the affected limb, demonstrated the insufficiency of the valves."

In 1869 Bryk[13] reported a somewhat similar case, dependent in part upon cardiac disease apparently acquired. A female servant, twenty years old, from her ninth year had had frequently recurring attacks of erysipelas of the left leg and foot, which in her sixteenth year eventuated in the establishment of an ulcer on the inner side of the ankle, followed by swelling and enlargement of the foot and leg, with horny and thorn-like excrescences upon the thickened and callous skin. "The heart was enlarged transversely, the area of dulness extending from the edge of the sternum to beyond the left nipple, and there was a systolic murmur at the apex. The liver extended the width of three fingers below the arch of the ribs; the spleen, as well as the submaxillary and, especially, the left inguinal glands, were enlarged and indurated." Busey[11] (pp. 139–140) quotes this case and relates that "the history of this case, as well as its course, apparently located the origin of the elephantiatic development in the lymphatic system. In view, however, of facts primarily presented the insufficiency of the mitral valves cannot be wholly excluded as a factor in producing the stasis of the lymph."

These two cases are quoted in detail because their histories and the elephantiatic conditions resemble the case herewith reported, particularly Cholmeley's case, in which there was no inflammatory condition as an exciting cause. Bryk's patient developed elephantiasis after repeated attacks of erysipelas, and the description of the scars on the affected limb suggests a difference in appearance, may be, sufficient to separate the enlargements due in part to infection and enlargements developing without infection. A second case quoted from Bryk[14] tends to substantiate this difference. A blacksmith, thirty years of age, gave a history of good health up to five years ago, when he suffered from erysipelatous attacks which developed in varices about the left knee-joint and later in the entire leg and in the arm. One year later the right leg was the location of an erysipelatous attack with abscess formation upon the leg and in the inguinal glands. After cicatrization of the inflamed parts at first the foot and afterward the leg "began to be thickened elephantiatically." . . . "With the exception of the funnel-shaped scars in the right inguinal region the skin of the thigh was

smooth, but in the leg were numerous scars, and in places the surface was uneven and rough on account of the densely crowded, hard nodes the size of nuts, not movable over adjacent parts . . . and furrowed by numerous rugæ passing in every direction." Sensibility was undisturbed. The glands were generally enlarged, but not painful. A strong systolic murmur was perceptible over the femoral artery of both extremities; the thoracic organs were healthy; no albumin was in the urine.

Continuance of bandaging alone reduced the volume, which increased when the bandage was not employed. After ten months the femoral artery was ligated below Poupart's ligament, "with the effect of reducing the limb to its normal dimensions in the course of two months, but another relapse soon followed."

Quincke[15] reported the following case in 1875: A woman of thirty years with "peritoneal dropsy"—effusion of chyle into the peritoneal cavity—developed œdema of the right leg and forearm and elephantiatic formation, probably due to disturbances of lymphatic circulation of the parts affected. The integument was tense, thickened, and the surface irregular; sometimes a clear yellowish fluid dribbled from integumentary fissures. A postmortem revealed "fatty degeneration of the heart," an inflammatory thickening of the mesentery, and cadaveric emphysema.

Of this case Busey says (p. 80): "An œdematous condition and elephantiatic formation of the right leg and forearm due to the mesenteric condition, viz., an inflammatory thickening of both folds of the mesentery and transformation of the interposed adipose tissue into tense connective tissue." This case is quoted to emphasize the possible development of an elephantiasis from circulatory disturbances of the blood and lymph channels, independently of local inflammation in the extremities. A year after Quincke's report Winckel[16] described a case of enlargement of the left lower extremity, similar to phlegmasia alba dolens, tense and painful, without fever, which developed during the existence of chylous ascites, from which was withdrawn by tapping a milky fluid containing filaria.

From 1878 to 1882 there are no good records of such cases in the literature. In 1882 P. zur Nieden[17] published an inaugural dissertation upon a case of lymphangiectasis with lymphorrhagia affecting the labia. His quotations and views in regard to the pathological condition are referred to under the Description of the Pathological Condition.

From 1882 to 1898 the literature contains no good records of non-parasitic elephantiasis. In 1898 Jopson,[18] of Philadelphia, reported two congenital cases, one at four years and one at one and a half years of age, which he considered the result of intrauterine infection and lymphangitis of the limbs. He recognized four types of the congenital condition, viz.:

Elephantiasis congenita lymphangiectatica;
Elephantiasis congenita telangiectatica;
Elephantiasis congenita fibromatosa;
Elephantiasis congenita neuromatodes.

Among the more recent cases are the following: Favarger[19] (1901) reported a case of non-parasitic elephantiasis due in part to a weak heart. The man, a native of Styria, twenty-five years old, was a farmer who had never left his native country. At fifteen years of age he suffered from a left pleural inflammation which recurred during the following two years. Œdema of both feet was noted at eighteen years of age, and later chronic eczema developed. The heart action was weak, the sounds were clear. The swelling and œdema in the left leg increased until they were enormous, and the scrotum, joints, and right leg below the knee were also swollen. Favarger thought this a sporadic case of elephantiasis, without a possibility of filarial invasion, resulting from a predisposition to chronic œdema readily satisfied by the "weak" heart action which maintained a cardiac stasis as well as lymph stasis, and infection with the cocci of erysipelas or other bacteria and subsequent increase in connective tissue.

In 1902 Rolleston[20] reported two cases of moderate enlargement of the legs in two patients, brother and sister, the condition being a peculiar œdema of the tissues which was permanent as long as they led an ordinary life; after exercise it increased, but disappeared after rest in bed for some days. He suggested that the persistent tendency to œdema from gravitation depends upon some inherent defect or peculiarity of the small bloodvessels, which allows of excessive transudation on slight provocation.

Pokrovski[21] (1902) reported two cases of elephantiasis due to syphilis and cited cases of syphilitic elephantiasis described by Minokoff in 1893 and by Orloff in 1901. Tchlenoff[22] in the same year described a case of elephantiasis of the vulva in a syphilitic woman thirty-eight years old, who had had seven miscarriages and had been under treatment for years. He thought some other factor besides syphilis necessary to produce the condition, but made no definite statement in regard to such factors.

A case of elephantiasis dependent upon a congenital defect in the lymph-vessel system of a male child, two years old, was reported by Bernhard and Blumenthal[23] in 1902. The child was admitted to the hospital for a deformity of the external genitalia. Shortly after birth an operation for phimosis was performed, and at this time the elephantiatic condition of the left foot was noted. After operation the prepuce swelled continuously and the entire left leg developed a condition of pronounced elephantiasis, both the external genitalia and the leg presenting a furrowed, greatly thickened skin. The left leg measured from 4 to 8 cm. more than the right in corresponding parts. Surface temperature and sen-

sibility were the same in the left and the right legs, but the surface of the left was drier and harsher on palpation. Microscopic examination of the tissue showed a diffuse fibromatous change in the connective tissue and marked lymphangiectasis. The family history was excellent and there was no history or evidence of an earlier inflammatory condition of the left leg or genitals. They thought the enlargement dependent upon some congenital anomaly of the lymph-vessel system. This case resembles Friedberg's case of colossal development of the right leg, in which, the condition was extremely marked at birth, however, and deformities of the skeletal as well as of soft parts existed.

Cases of elephantiasis have been reported not infrequently in the United States, some of them parasitic in nature and imported from tropical countries where filariasis is endemic. In recent years I have seen four cases of filariasis, early cases with no change in the subcutaneous tissues.

The case here recorded seemed to me to be one having as etiological factors the chronic cardiac condition and some local lymphatic deficiency in the right leg. The history does not make clear the duration of the cardiac disease, but does exclude the probability of parasitic invasion, and the normal blood condition bears out the history. I am aware of the fact that in parasitic elephantiasis filaria embryos are rarely found in the blood. (Manson's *Tropical Diseases*, 1899, p. 466.) Entire freedom from attacks of inflammation in or repeated injuries to the right leg suggested that the local condition depends upon some defect in the lymphatics of the part affected, whether congenital or acquired it is difficult to prove. The occurrence and persistence without steady increase in size of an œdematous condition of the left leg suggest more strongly some local lymph-vessel deficiency in the right leg. The repeated occurrence of œdema during three pregnancies and the cardiac disease with several periods of broken compensation would account for the œdema in both legs, and yet not for the thick, elephantiatic condition of the skin of the right leg. The case corresponds closely to the cases of Cholmeley and Quincke, quoted from Busey's monograph, cases which Busey considered due to latent congenital defect combined with accessory causes later in life, thereby producing an acquired condition depending partly upon a congenital defect.

C. W., a native of the United States, twenty-eight years of age, by occupation a silkwinder, was admitted to the Medical Dispensary, March 13, 1902, complaining of pain in the left arm and left chest.

Family History. Parents are living; mother has suffered from "Bright's Disease" and dropsy" for years; one sister has heart disease and has been under observation at the Dispensary for mitral stenosis; one brother died of consumption at twenty-four years of age; other brothers and sisters died in infancy.

Personal History. The patient was born in Freehold, N. J. When an infant the family moved to Chicago, thence to Philadelphia, thence to New York, eighteen years ago, and the patient has never been out of these four States. No illness occurred in childhood excepting measles. During the last three years she has been questioned occasionally in regard to early illness and important details, and the history given in 1902 is correct. Excepting measles, there is absolutely no history of infectious disease or of local infection. Menstruation was established during the eleventh year, and when seventeen years old she married. Five years after marriage she had been the mother of four children, one of whom died of meningitis, a second of diphtheria, a third at two weeks of age from an undetermined cause, and the fourth is living and in good health. Her husband died of pulmonary tuberculosis six years after their marriage. With each of the four pregnancies there was moderate bilateral œdema of the legs, no more marked in right than in left, but never a permanent swelling of either leg after pregnancy. During no one of the pregnancies were there signs or symptoms of femoral vein thrombosis or inflammation of the legs, and the condition of the limbs above the knee confirmed the statement. There was no fever or illness following parturition. After her husband's death she began work as a silkwinder, which necessitates constant walking to and fro, and within two years' time the right ankle began to swell during the day, the swelling subsiding at night, and gradually over a period of one and a half years the leg below the knee became much enlarged. For four years the permanent swelling has been slowly increasing.

There has been no urinary disturbance and the urine has never been milky.

Present Illness. Four days before admission (March 13, 1902) she was suddenly taken with a sharp, darting pain in the lower left chest, which after from two to three hours extended to the left arm and was sufficiently severe to prevent sleep. There was dyspnœa after exertion. For two weeks the left chest had felt uncomfortable and the left foot had swollen. There was "increased" urination; no cough.

Examination. The lower eyelids were puffy, the pupils dilated, and the eyes deeply dark-ringed. The tongue was lightly coated. Thorax well formed, sternum straight, and lungs normal throughout.

Heart. The apex-beat was visible in the fifth space 10 cm. from the midsternum; the maximum impulse was 11 cm. from the midsternum in the fifth space, well outside the midclavicular line. There was no thrill and the shock of the first sound was felt. The area of relative cardiac dulness was enlarged to the left and extended not quite to the sternal border to the right. Cardiac pulsations were 114 to the minute. At the apex a blowing

systolic murmur, soft and of short duration, was heard; in the fifth space, from 11 to 12 cm. from the median line, there was a loud rumbling diastolic murmur, not constant; and mesial to the maximum impulse a loud, high-pitched blowing diastolic murmur was constantly heard; this murmur increased in intensity toward the aortic area, was audible though less distinct at the left of the sternum in the second interspace, and loudest in the third and fourth interspaces to the left of the sternum. The tricuspid area was clear. The second aortic sound was obliterated, the second pulmonic sound was not accentuated. The pulse was full, large, quick, not

FIG. 1

To the right, C. W., aged twenty-eight years, the subject of non-parasitic elephantiasis, aortic insufficiency, and rheumatic purpura. To the left, M. A., aged twenty-four years, a sister of C. W., and a subject of mitral stenosis (the legs and thighs normal). Photograph taken March 27, 1902.

typically Corrigan. There was a well-marked capillary pulse in the finger nails, and a well-marked Riesman-Müller sign upon examination of the throat.

The right leg from the knee down was greatly enlarged, measuring 58 cm. in the largest circumference in the middle third of the calf; the enlargement was fairly regular and uniform (Fig. 1). The surface was smooth, with the exception of a pitted area 2 cm. in diameter, suggesting a scar near the lower third anteriorly, and exaggeration of the skin folds near the ankle. Over the posterior surface (Fig. 2) were scattered six small pitted areas, the skin covering which was

in no way different from that over the remainder of the leg. The skin was markedly thickened, boggy, but not tense, and did not pit on pressure as did the simple œdematous left leg, nor was the skin rough and harsh as in filarial elephantiasis. There was no local temperature, no swelling, no tenderness. The hair overlying the anterior surface particularly was long and had been "frequently cut off." The patient stated that after standing or walking the right leg was as hard as a rock and the bandage worn about the swollen calf became "saturated with water." Scattered over the surface were a few dilated venules. The left leg presented a moderate œdema and some thickening of the soft parts, and also a pitted scar over the lower third anteriorly. The greatest circumference of the left calf was 34 cm. The œdema existed over both feet and in the left limb up to the lower third of the thigh. The bony structures about the right knee-joint were evidently enlarged and thickened, particularly the condyles of the tibia.

The thickening of the skin did not suggest scleroderma.

Abdominal Examination. Pelvic and abdominal examinations were negative. The cardiac condition was treated, with no change in the size of the right leg, but with partial disappearance of the œdema in the left leg.

The history and the preceding examination were recorded on March 13, 1902. Two weeks later, on March 27, she returned, with a history of pain and soreness across the abdomen for three or four days, some pain in both knees, ankles, and bones of the forearms. There was no chill, no fever, no vomiting or nausea, but sweating and severe headache. There was no bleeding from the nose, mouth or bowel, and the urine had been normal in color. Thirty-four hours before the visit and two days after the onset of pains in the joints she suffered from a sudden attack of intense pain in the left side of the abdomen, and bright-red spots appeared on the thighs and upper legs, most abundant about the knees, also on the dorsal surfaces of the forearms and wrists. On examination the spots were dark purple-red, in size from 1 mm. to a blotch from 2 to 3 cm. in diameter. The knee-joints and inner sides of both thighs were tender. The swelling of the legs had not changed.

The abdomen was tender in the upper zone, otherwise negative. The lungs were normal.

The cardiac area had decreased, the maximum impulse being 9.5 cm. from the midsternum in place of 11 cm. on March 13th; the loud diastolic aortic murmur replaced the second aortic sound and the pulmonic second sound was intensely sharp and accentuated. The pulse was 90 to the minute, quite regular in rhythm and force.

At this visit the photographs were taken, and the purpuric spots are clearly defined (Figs. 1 and 2).

The two blood examinations had shown a normal blood condition, with the exception of a slight increase in the erythrocytes; hemo-

globin, 88 per cent.; red blood corpuscles, 5,600,000; white blood corpuscles, 8000. Differential count of the leukocytes (300): polymorphonuclear, 71 per cent.; lymphocytes, 21 per cent.; large mononuclear, 8 per cent.; eosinophiles, 0 per cent.; mast cells, 0 per cent.; parasites not found.

January 19, 1904. The patient returned after an absence of twenty months, with the following history: On June 10, 1903, after a fall, when she bruised the inner side of the enlarged right calf, "gangrene set in." She was taken to a hospital and remained there three months, until September, 1903, since when she has visited the hospital twice weekly to have the last wound dressed.

FIG. 2

Rear view of C. W., non-parasitic elephantiasis.

Three operations were performed under cocaine. At the first "pus" was obtained, but later the discharge became serous, as it is at present. At the time of the operations her medical attendants stated that the skin was one and one-half inches thick.

She complained again, (January 19, 1904) of dyspnœa, aching in the arms and thorax, and of excessive "pounding" of the heart. General health had been excellent. The œdema of the left and enlargement of the right leg had not increased. The cardiac area had again extended, there was a diastolic rumbling murmur at the apex in the fifth interspace from 10 to 11 cm. from the midsternum, and a loud diastolic aortic murmur most intense in the third and

fourth spaces along the left sternal border. The tricuspid area was clear. The pulse was large, quick, regular in rhythm. The lungs were normal. Abdominal examination was negative.

The œdema of the left leg about the ankle was moderate. The dressing about the right leg below the knee was wet with a sticky, serous fluid. There was no thickening or dilatation along the veins of the right leg, and nothing abnormal about the genitalia.

The measurements of the two legs were:

	Right.	Left.
Ankle	26 cm.	18 cm.
Two inches below knee	44 cm.	
Three inches above knee	37 cm.	
Largest measurement of calf		36 cm

Above the right knee, in lower third of thigh, the skin was slightly thickened. The left leg was œdematous from knee to ankle, and œdema extended to both feet. The right leg had become much reduced in size, the largest measurement of 44 cm. being 14 cm. less than the 58 cm. of March 13, 1902.

The patient's last visit was in March, 1905, for the cardiac condition, and at that time the operation wound of June, 1903, had not healed, the condition being that of a fistulous opening discharging serous fluid, similar to the conditions of lymphorrhagia or lymphorrhœa recorded by Busey,[10 11] by Fischer,[24] and by P. zur Nieden.[17]

This constant discharge of serous fluid undoubtedly accounts for the reduction in size of the right leg, from 58 cm. in 1902 to 44 cm. in 1904 and 1905. At no time has a milky discharge been noted, although she was requested to look for it. The serous discharge has in no way affected her general health, which is good. She still follows the occupation of silkwinder, and responds readily to treatment when the cardiac condition loses its compensation.

It has not been possible to obtain a section of tissue for histological study. There seems no doubt, however, that the condition is dependent upon the repeated œdema during four pregnancies, leading to dilatation and may be insufficiency of the valves of the lymph vessels, the cardiac disease, with its consequent attacks of stasis, the patient's standing occupation, and possibly some congenital deficiency of the lymph-vessel system of the right lower extremity. History and evidence of infection are wanting, and fortunately infection has not occurred since the operations in 1903.

Aside from bandages properly applied, rest with elevation of the limb when possible, and massage, the treatment has been directed to the cardiac disease.

DESCRIPTION OF THE PATHOLOGICAL CONDITION.

Allard,[4] in a brochure entitled "De l'inflammation des vaisseaux absorbant lymphatique" (Paris, 1824), defined elephantiasis as

a "chronic inflammation of the lymphatics of the affected part and ultimately of the remainder of the body."

Busey[16] accepted Virchow's description of the changes in the tissues and recognized an elephantiasis dura, in which a connective tissue of stiff, glistening, white fibers, very firm and almost scirrhous, was found in place of the soft parts; and an elephantiasis mollis, in which the enlarged parts consisted of a soft, gelatinous, uniform tissue. Busey quoted Kaposi as stating that the two changes were not indicative of distinct diseases, and again quoted Kaposi and Tillbury Fox in regard to the fluid found in these tissues, the former considering it a "fibrinogenous" substance, the latter stating it to be lymph.

P. zur Nieden[17] in a monograph considers in detail the genesis of elephantiasis depending upon lymphangiectasis resulting from inflammation. With the initial and prodromal erysipelatous skin inflammation the lymph vessels and glands take part, and thus thrombosis of the lymph vessels and blocking of the glands due to cell-growth accounts for a mechanical lymph stasis. Retention of "tissue juice" is a source of irritation and furnishes material for hyperplasia. Quite the contrary is Wernher's[25] view that the lymph vessels in no place, either capillary or in the glands, are blocked, but the stasis of lymph has ground only in the varicose dilatation, and hereto is the elephantiasis secondary. As a cause for varicosities (lymphatic) Wernher considers gravity the first, as with venous varices. Lallement[26] accepts an atony of the lymph-vessel wall in consequence of repeated erysipelatous attacks as the most important etiological factor. Schliz,[27] after examining the skin from a case of elephantiasis, concluded that the obliteration of lymph vessels of deeper layers occurred through endothelial growth of the walls, and he quotes Virchow[28] as noting the similar endothelial growth in elephantiasis without an explicit statement as to obliteration. Rindfleisch,[29] in a case of pachydermia lymphangiectatica scroti, found a hyperplasia and neoplasia of musculature, and thought the lymph-vessel branches to be compressed by contraction of this muscle. Nieden could not explain the absence of elephantiasis in cases with well-marked lymphangiectasis. Nieden's article contains sixteen careful analyses of lymph from cases of lymphorrhagia.

Jarisch[30] in *Nothnagel's System* describes elephantiasis as resulting from a chronic circulatory disturbance particularly of the lymph system or thoracic duct, accompanying and beginning in acute inflammation and resulting in hyperplasia of the subcutaneous connective tissue. The condition (p. 839) often depends upon recurrent erysipeloid inflammations, phlebitis from lupus, syphilitic ulcerations, ulcers of the foot, and filarial invasion. All of these acquired forms are classified under elephantiasis arabum and separated from the congenital forms, viz., elephantiasis telangiectatica, ele-

phantiasis lymphangiectatica, and the neurofibromatous conditions. The acquired elephantoid condition occurring without inflammation is not mentioned.

Neisser and Jadassohn[31] state that with venous stasis there occur purulent inflammation and connective-tissue hyperplasia of the lymph-vessel system, resulting in the condition called elephantiasis, particularly after recurrent erysipelas (p. 74). Often a true elephantiasis follows a ring-ulcer of the leg. Three forms are recognized, all consisting of a chronic hyperplasia of subcutaneous connective tissue, with more or less œdema and venous hyperæmia:

(*a*) Elephantiasis nostras;

(*b*) Elephantiasis of tropical regions;

(*c*) Elephantiasis-like forms of connective-tissue tumor occurring as congenital deformities in contrast to the acquired forms (*a*) and (*b*).

Elephantiasis nostras results from a chronic or recurrent inflammation combined with stasis in the lymph- and bloodvessels occurring with chronic eczema, chronic ulcerations, lupus, syphilitic tumors, phlebitis, lymphangitis, and particularly with erysipelas due to the streptococcus (Bockardt). Sometimes (p. 227) chronic œdema without history (carefully taken) of earlier erysipelas (although erysipelas may be afebrile and mild; Reclus' "Halzphlegmonie" equals bacterial infection without fever) may be the apparent cause; and more rarely the condition may be postoperative or neuropathic, with neuritis or paraplegia. This type (*a*) affects usually the legs; more rarely the arms, scrotum, labia majora, and the face in tuberculous and syphilitic conditions. There is also a form (p. 229), not to be confused with (*c*), which is congenital in origin, due to intrauterine streptococcus infection of the fœtus from an erysipelatous mother.

The tropical form (*b*) is due to Filaria humani. The group (*c*) of congenital connective-tissue tumors, or tumors having a congenital "grundlage," best called fibromas, are often boggy and tumor-like thickenings of the skin, of which three types are to be recognized:

Elephantiasis telangiectodes;

Elephantiasis lymphangiectodes;

Elephantiasis with involvement of the peripheral nerves, equal neurofibroma. ("Dystrophie œdémateuse héréditaire" and "trophœdéme chronique héréditaire".)

Clinically (p. 227) the four following conditions are to be recognized:

Elephantiasis glabra (smooth);

Elephantiasis nigra (spotted and dark);

Elephantiasis verrucosa sive papillaris;

Elephantiasis lymphangiectodes (with lymphorrhœa).

Fischer's[24] monograph in one part (1901) discusses thoroughly all phases of disease of the lymph vessels, and for a complete bibliography the reader is referred to his publication (pp. x–xiv). At the end of the eighteenth century the normal anatomy of the lymph-vessel system had been carefully described by Henson, Mascagni,

and Cruikshank; and Assalini and Sömmering had explained disease processes on the theory of interruption to the flow of lymph through the lymph-vessel system. Later, Allard and Andral concluded the disease processes to be due to inflammation, and this view was upheld by the French school—Velpeau, Breschet, J. Roux, Chassaignac.

During the last eighty years acute inflammation, tuberculosis, and malignant tumors of the lymph vessels have been reported. Fischer separates the acute infectious conditions into two groups, *A* and *B:*

A. Lymphangitis superficialis,

1. Lymphangitis truncularis (ascendens).

(*a*) Simple acute form;

(*b*) Purulent subacute, involving the larger collected bundles of vessels, in surgical blood poisoning and glanders.

2. Lymphangitis reticularis, involving the net-work of vessels in the skin: subepidermal, dermal, or subdermal lymph vessels, conditions often not distinguishable from erysipelas, although they develop no indurated line of demarcation as does erysipelas; and

3. Lymphangitis gangrenosa.

B. Lymphangitis profunda, involving the deeper tissues.

The chronic inflammatory conditions are not specific but result from failure to destroy the source of irritation from an old infection in ulcers and chronic inflammations leading to recurrent lymphangitis. Fischer recognizes two types, viz.:

(*a*) Reticularis (chronic);

(*b*) Truncularis (chronic).

The course of chronic inflammation of large vessel trunks is without pain. The lymph circulation of the area affected is hindered and the collateral circulation is not in function; this condition results in an œdematous swelling peripheral to the area in which the lymph vessels are blocked, sometimes with lymphangiectasis. Particularly if deprived of treatment are the cases of "Strang" (ascending), lymphangitis prone to result in "elephantiatic" changes, since the walls of the vessels, closed by endothelial hyperplasia or by thrombi, undergo a fibrous connective-tissue degeneration which involves the neighboring and enclosed connective tissue and the smaller vessels, particularly the smaller veins.

Dilatation of the lymph channels, *i. e.*, lymphangiectasis, and the formation of lymph varices and lymphangiomas are often congenital afflictions, appearing with birth or soon after birth. (Fischer quotes Patterson and Busey.) The development of lymphangiectasis may occur later in life and these cases fall into two groups, separated etiologically into

A. The tropical, due to invasion of the lymph channels by filaria sanguinis;

B. The non-parasitic, spontaneous, or after occlusion of lymph channels.

This group of cases has its origin in an external or internal obstruction to the on-flow of lymph from the distal portion of a part, in consequence of which the lymph-vessel content is under abnormally high pressure, so that a bulging of the wall occurs. Interruption of the stream can give rise to contracting pathological changes resulting in marked narrowing of the lumen.

Repeated (recurrent) lymphangitis and erysipelas lead to thrombosis and complete occlusion; or complete occlusion may result from neoplasm of parts (cancer, Richet), or from endothelial hyperplasia (C. O. Weber), or from chronic infection (tuberculosis, Goupil), or from invasion by parasites (Filaria, Lewis, Mazéa-Azema, Scheube). Occlusion may result from external pressure after injury and inflammation which in healing have left a contracting, shrivelling, extending scar (Patterson, Klebs); from tumors gradually increasing in volume in the neighborhood of vessels (Busey); in extensive ascites (Know and Egger). Destruction of lymph-vessel area from acute and chronic suppuration of lymph glands, after extirpation of glands, trauma directly affecting the vessels, as in fracture, extensive section of the soft parts (Trélat, Ledderhose) can lead to obstruction to on-flow and subsequently lymphangiectasis. To other authors the difficulty of reflux of lymph into the venous system, arising from abnormally high pressure in consequence of heart disease, congenital stenosis of the venous ostia, and other obstructions to the circulation, suffices to explain the development of dilatation. In such cases the dilatation is confined to the thoracic duct and the large trunks of the thorax and abdomen (Rokitansky, Löschner), or more rarely the peripheral lymph vessels may also become dilated, particularly those of the thigh and genitals (Petters, Simon). Wright believes that the development of lymph varices may depend upon an abnormal increase of vessel content, without previous inflammation of vessels or glands. Bean and Emmert consider paralysis of the muscularis of the larger lymph vessels a possible cause of dilatation. Unna considers the lymph-vessel dilatation the result of two factors, a hindrance to lymph-flow and to blood-flow, the latter being a pressure which works against the natural blood stream, leading particularly to stasis of neighboring veins. Stasis and retention of lymph do not always lead to dilatation, for collateral circulation may be good. Experimental stasis of ductus and larger vessels does not always lead to dilatation (Magendie, Dupuytren, Conheim); obliteration of the vessels of an extremity does not result in lymphangiectasis (v. Lesser); nor does dilatation often follow extirpation of glands. Accordingly, Langhans, Torock, and Nasse take the view that proliferation processes in the lymph-vessel walls play the greatest part in the production of dilatation.

Fischer does not lay much stress on proliferation processes, but takes the view of v. Esmarch, Kulenkampf, and others, that lymph

varices arise only when vessels over a large area are obstructed, are overfilled, and the wall elasticity is thus injured and the valves become inefficient, either from dilatation alone or from inflammatory changes.

One may compare these with venous varices and accept a congenital "anlage," which is to be looked for in an abnormal width and flabbiness of the lymph-vessel walls, which readily lend themselves to the development of dilatation through stasis.

The two forms of lymphangiectasis, (1) reticularis, and (2) truncularis, often occur together.

1. Lymphangitis reticularis consists in a dilatation of vessels and capillaries (and "Wurzelgebiete") leading to a "pachydermia lymphangiectatica," in which the outer epidermis is the primary site, the hypertrophic process in the cutaneous and subcutaneous tissues resulting secondarily from the irritation arising from the primary lymph stasis (Kulenkampf, v. Winiwarter, A. Fischer, Teichmann).

On the normal thickened, sometimes pigmented, skin one finds small blebs, which, after being emptied of their fluid contents, have a sharply defined border. On section one sees close under the papillary layer endothelial cell spaces and widened papillary lymph spaces communicating with a net-work of dilated lymph vessels in the skin and subcutaneous tissue. The "spaces" extend to the point of the papillæ and are separated from a thin epidermal by a thin connective-tissue layer, in some more extensively dilated; the connective tissue is atrophied so that the endothelium is in contact with the epidermal layer; the content of the spaces is usually fluid, sometimes with finely granular net-work masses—the coagulated lymph—which contains the few nucleated lymphoid cells. The sebaceous and sweat glands and hair follicles as well as the papillæ are compressed, whereby atrophy of these structures arises. Bloodvessels completely unchanged or dilated project as bulgings into the spaces; through rupture of these vessels the contents became sanguineous. In the papillary and subcutaneous layers irritation is evidenced by a variable high grade of round-cell infiltration.

2. In lymphangitis truncularis the vessels above and below the fascia of the part are involved; either small sections of a trunk are partially dilated, or the dilatation extends along the whole length in a cylindrical or serpentine form. Changes in the vessel wall at the dilated area show lack of growth of the muscularis (Anger). Nieden states the contrary, but the musculature is strong in growth in the slightly dilated portions; clear statements are wanting in regard to the relations of endothelium, intima, and elastic fibers. The number of valves is lessened, the length of those present reduced and insufficient, whereby the turgescence of the varices on standing and walking occurs without hindrance. The widening, bulging, and thickening of the vessel walls occur most often without symptoms.

The dilated lymph vessels at times can be rolled under the fingers. Often lymphorrhagia or lymphorrhœa is the first symptom or sign, the fluid amounting to a few grams or many pounds in a day. Pressure below a fistula in such a case, on standing, increases the flow. The output depends in part upon the opening, often small and fine (Klebs and Tillmann), or may be a flow or exudation from between the epithelial cells (as in the case here reported) without a fistulous opening, and again large fistulæ which admit a sound and communicate with large spaces. Thus one may find normal skin, or more or less pigmented, hypertrophic, elephantiatic changes in the skin, with small flaxseed or pea-sized simple or confluent blebs which contain clear, milky, or sanguineous fluid. The fluid is lymph and related to chyle (Neiden, v. Esmarch, Kulenkampf). Excessive loss of it may lead to emaciation, weakness, and death. Munk and Rosenstein reported a case with a fistula on the inner side of an elephantiatic left leg, which in hunger discharged a clear, slightly opalescent fluid, and after digestion of a fat meal a milky fat-droplet chyle. These varices of lymph vessel net-work may extend over an entire extremity; in such cases hypertrophic changes in the subcutaneous connective tissue result in elephantiasis (v. Winiwarter).

I am indebted to Dr. E. S. Loiseaux, of Morristown, N. J., for the following account of the condition found at operation.

"S. W. was admitted to the hospital with a subcutaneous abscess in the right leg posteriorly. The abscess was secondary to a skin abrasion, received over its site two weeks previously to admission. On incision the skin itself was very much thickened and the pus cavity was several inches in diameter and two or three inches deep, possibly a little more.

This cavity seemed to be immediately beneath the skin proper, in the superficial fascia—I could not say that it extended down to the deep fascia. The skin itself was about three-eighths of an inch thick and its toughness kept the abscess from spontaneous evacuation.

As far as the hypertrophy is concerned I should say that it was nearly all in the superficial fascia or subcutaneous tissue. . . I considered the whole condition one of lymphœdema, as it appeared in the puerperal period. At this time the blood was examined night and day for filaria and none were found."

With Dr. Loiseaux I believe the condition dependent in part upon "lymphœdema" of pregnancy, and the subsequent hypertrophy of the skin and subcutaneous tissue, in the right leg and not in the left, due to chronic lymph stasis dependent upon lymph-vessel deficiency, probably congenital, as suggested by the earlier observers quoted in this article.

Unfortunately it has not been possible to obtain tissue for microscopic examination.

BIBLIOGRAPHY.

1. Morgagni. De sedibus et causis morborum, Liber ii, p. 152, Venice, 1761; Liber iii, 26. Translation by Alexander, London, 1769, p. 300.
2. Chevalier. Medical and Chirurgical Transactions, London, 1817, vol. ii, p. 63.
3. *Kennedy. Edinburgh Medical and Surgical Journal, 1817, vol. xiii, p. 54.*
4. Quoted by Hasse: "Diseases of Organs of Circulation and Respiration." Translation by Swaine, Sydenham Society, London, 1846, p. 7.
5. Wormi. Gazette Hebdomadaire, vol. vi, p. 279, 1859.
6. Turner. Edinburgh Medical Journal, 1859, p. 1003.
7. Demarquay. Gazette Medicale, Paris, 1863, xviii, p. 665.
8. T. R. Lewis. "The Pathological Significance of Nematode Hematozoa," Calcutta, 1871.
9. Jackson. Transactions of the Pathological Society of London, 1866, xvii, 287.
10. Busey. "Congenital Occlusion and Dilatation of Lymph Channels, 1878, p. 165.
11. Busey. "Narrowing, Occlusion, and Dilatation of Lymph Channels, Acquired Forms," 1878.
12. Cholmeley. Transactions of Clinical Society of London, 1869, vol. ii, 116 Quoted by Busey, p. 136.
13. Bryk. Oesterreich, Zeit. f. Heilkunde, 1869, 469.
14. Bryk. Ibid., 449.
15. Quincke. Deutsche Archiv f. klin. Med., 1875, xvi, 128.
16. Winckel. Ibid., 1876, xvii, 303.
17. P. zur Nieden. "Ueber einen Fall von Lymphangiectasie mit Lymphorrhagie," Berlin, 1882.
18. Jopson. Archives of Pediatrics, 1898, 174.
19. Favarger. Wiener klinische Wochenschrift, December 26, 1901.
20. Rolleston. Lancet, September 20, 1902.
21. Pokrovski. Medicinskoie Obozrenie, 1902, lvii, No. 8, from Philadelphia Medical Journal, November 8, 1902, 570.
22. Tchlenoff. Medicinskoie Obozrenie, 1902, lvii, No. 11, 859, from Philadelphia Medical Journal, December 27, 1902, 1039.
23. Bernhard and Blumenthal. Deutsche med. Wochen., December 11, 1902, p. 902.
24. Fischer. Deutsche Chirurgie, 1901, Lief. 24 a.
25. Wernher. Deutsches Zeit. f. Chirurgie, 1875, v, 429.
26. Lallement. Cited by Schliz, Archiv f. Heilkunde, 1874, xv, 153.
27. Schliz. Loc cit., p. 163.
28. Virchow. "Die Krankhaften Geschwülste," Band i, 303.
29. Rindfleisch. Lehrbuch der Pathologische Gewebeschre, 1871, 2 auf. 277.
30. Nothnagel's Specielle Pathologie und Therapie, 1900, Band xxiv, 714.
31. Neisser and Jadassohn. Ebstein und Schwalbe, Handbuch der Praktischen Medizin, 1901, iii, 29.
32. v. Winiwarter. Deutsches Chirurgie, Lief. xxiii, 355–402.

RESULTS OF THE BITERMINAL TRANSPLANTATION OF VEINS.

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AND

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THE first series of experiments performed demonstrated that by interposing between the two cut ends of an artery a segment of vein it is possible to restore quickly the arterial circulation, and that the venous segment is able to perform the principal arterial functions. A summary of the immediate results of this operation,

together with the main conclusions to be drawn therefrom, have already been published.[1]

After finding that a venous segment transplanted on the arterial apparatus adequately supported the blood pressure, we tried to determine to what extent such a segment would acquire arterial characters. It is well known, indeed, that the function and development of an organ are intimately associated, and that even in adult animals an organ or tissue may be caused to undergo extensive anatomical and physiological development. It might be assumed, therefore, that a vein acquiring the functions of an artery would become arterial in all its characters. But as we believe this method of transplanting veins may be used in man, as in the treatment of large wounds of arteries and aneurysms, we consider it necessary to determine carefully the permanent effects of the arterial blood pressure on the venous wall, before this application is made.

A second series of experiments was performed. Three dogs were operated on under aseptic technique. Two of the animals were etherized and the results of the operations studied six and fourteen days respectively after the operation. The third animal was kept alive. By examining it over a long period of time it may be possible to determine the permanent results of the operation.[2]

EXPERIMENT I. Transplantation was made of a segment of the femoral vein between the two cut ends of the femoral artery. The ends of the venous segment were dissected and transplanted on the artery, but all the middle portion was permitted to retain its normal connections, including its collaterals. After the circulation was re-established these collaterals became similar to small collateral arteries. It was therefore an incomplete biterminal transplantation.

EXPERIMENT II. Complete biterminal transplantation was made. A long segment of the external jugular vein was dissected out and completely extirpated and put in a glass of isotonic sodium chloride solution. Afterward the carotid artery was dissected and severed. The venous segment was interposed between and united to its cut ends, and the circulation re-established.

EXPERIMENT III. Same as Experiment II.

PHYSIOLOGICAL RESULTS. Immediately after the re-establishment of the circulation in an artery after the interposition of a segment of vein in its course the circulation through the portion of the artery peripheral to the venous segment is somewhat modified, the pulsations being weaker. In a case of interposition of a very long segment of the jugular vein, between the cut ends of the carotid

[1] Anastomosis and Transplantation of Bloodvessels, Amer. Med., 1905, vol. x, 284, 1101.

[2] This paper has been delayed in transmission. Since it was written numerous vascular transplantations have been performed. These operations have shown that the arteriovenous anastomoses remain in excellent condition twelve months after the operation, and that the modifications of the venous wall are constant and proportional to the increase of blood pressure. All the subsequent observations have confirmed the results given in this paper.

artery with excellent restoration of circulation, the pulsations of the artery distal to the segment were almost imperceptible to the touch, while between the segment and the heart the pulsations were strong. Manometric tracings of the arterial blood pressure and pulse central and distal to the venous segment showed marked differences in the case of the pulse, the distal tracings being the weaker, while the blood pressure was the same in both cases. This effect on the pulse was probably due to the semicircular shape the segment assumed, owing to its great length compared to the length of the interval it occupied between the ends of the artery. These observations were made about two hours after the operation. In order to ascertain what changes, if any, take place in the circulation longer intervals after the operation, the animals aseptically operated upon are being studied.

The first dog was examined the fifth and sixth days after the operation. The pulsations of the distal end of the femoral artery remained weaker than the pulsations of the corresponding point of the femoral artery of the other limb.

The second dog was examined the fifth, the thirteenth, and the fourteenth days after the operation. On the fifth day the pulsations were markedly weaker distal to the venous segment than between it and the heart, but on the thirteenth and the fourteenth days no difference in the pulsations on the two portions of the artery could be detected by a clinical examination. Immediately after this examination the animal was etherized and the artery exposed and dissected from the surrounding tissues. Direct examination confirmed the results of the clinical or external examination regarding the similarity of the arterial pulse above and below the venous segment.

Blood pressure and pulse tracings taken from the artery distal and central to the segment and recorded by a mercury manometer revealed no difference in the former and only slight differences in the latter.

It may, therefore, be concluded that the physiological differences in character of the arterial circulation distal and central to the venous segment present immediately after the operation are soon modified. This indicates the occurrence of adaptive anatomical changes in the segment.

On the third dog, the pulsations of the venous segment were easily detected by palpation and its wall seemed greatly thickened.[1]

ANATOMICAL RESULTS. *Macroscopic Examination.* The anatomical changes in the wall of the venous segment probably begin very soon after the operation, but for some days they cannot be detected macroscopically. On the sixth day the venous wall

[1] At the present time, eight months after the operation, this dog is in excellent health, and the circulation is very active through the venous segment, which to the touch exhibits the characteristics of the carotid artery.

which is a conservative assumption, the changes are enormous. For our present purposes, absolute measurements are unimportant, only *progressive or regressive* changes, *relative dimensions* and *tissues involved* in the changes being considered the points essential to determine.

Arterial Part. Beginning at the portion of the artery appearing in the specimen farthest from the point of anastomosis, the wall was 0.71 mm. thick and normal. The thickness and structure remained the same until a point about 5 mm. from the point of anastomosis was reached. Then the thickness began gradually to increase until at the point of anastomosis it was 1.19 mm. From this point back to the point where the thickening began, a wedge-shaped layer of granular material, in which were embedded scattering cells and fibers, was present between the middle and outer coat of the vessel. This largely accounts for the increase in thickness, the base of the layer of granular material being about 0.45 mm. wide.

The intima of the artery appeared normal. At the point of union with the venous segment it was bent outward with the middle coat toward the adventitia and appeared to form an anatomical union with the intima of the venous segment which was similarly bent. It was difficult to detect the exact relation of the intimas to each other, owing to the highly organized patch of fibrin present at the point of union.

The tunica media of the artery appeared to consist of an inner portion 0.28 mm. thick, composed of muscle fibers and elastic tissues, and an outer portion 0.09 mm. thick, mainly consisting of densely arranged elastic fibers, the total diameter of the coat being 0.37 mm. The reason for considering the outer layer of elastic tissue as a part of the middle coat is that the separation of the coats caused by the layer of granular material before mentioned occurred between this and the outer layers. Possibly it represents the layer sometimes described as the tunica elastica externa of Henle. The muscular layer ended near the point of anastomosis, by losing its muscular fibers, the elastic fibers becoming very densely packed and ending in a whorl around the silken ligature present in the end of the artery. The coat of fibrous tissue just external to the muscular coat also sent some fibers to join the whorl about the ligature, but for the most part the fibers ended abruptly. The corresponding coats of the wall of the venous segment ended very similarly around the ligature in its end, and the two whorls of fibers thus formed were connected by a well-developed band of fibers, which appeared to be continuous with the fibers in the inner portion of the muscular layer of the artery.

The tunica adventitia composing the remainder of the thickness of the arterial wall consisted mainly of connective-tissue fibers. In a zone near the outer margin of the coat, the fibers appeared denser, and among them were intermingled some elongated cells having

layer much. In the region of the anastomosis this layer became very prominent, the fibers much denser, and the nuclei more numerous. It was continuous with a similar layer in the outer coat of the venous segment.

The results obtained were based on the macroscopic examination that the wall of the artery was practically unaltered, except immediately at the point of anastomosis.

Vein. At the point of anastomosis the wall of the venous segment was approximately of the same thickness as the wall of the artery. From this point it very gradually increased in thickness for about 1.7 mm., at which point it was 1.57 mm. thick, which is slightly more than the thickness of the normal arterial wall. From this point it increased in thickness until a point about 6.0 mm. from the anastomosis was reached, where it was 2.88 mm. thick. From this point to the end of the specimen the wall was practically uniform in thickness.

The intima appeared uniform, being very similar to that of the artery in thickness. In the region of the anastomosis it was beneath the patch of fibrin and appeared to terminate, as before described, by uniting with the intima of the artery. The patch of fibrin measured 2.75 mm. in the longitudinal direction of the vessel and 0.48 mm. in thickness at the thickest point, which was near the point of anastomosis. It tapered gradually to a point at the other end. It appeared to be highly organized, consisting of a mass of cells which a band of fibers, about 0.22 mm. broad, and mainly from the muscular layer of the middle coat of the artery and vein, penetrated for some distance. The presence of these fibers rendered a definite statement as to whether or not the two intimas were directly united impossible, as they occurred at the point where the inner coats came the nearest together. In the centre of the organized mass an area 0.22 mm. by 0.64 mm., composed mainly of what appeared to be homogeneous blood pigment, occurred. This was the only sign of retrogressive change that could be detected. The free surface of the mass was absolutely smooth and regular.

The tunica media of the segment appeared to consist of two layers: an inner composed of muscle cells and longitudinal elastic fibers, and an outer consisting mainly of coarse, longitudinal, white connective and elastic fibers. In neither case were these layers as dense as the corresponding layers in the artery. At the point 1.7 mm. from the anastomosis the muscular layer was about 0.11 mm. thick and the fibrous layer 0.51 mm. At a point about 11 mm. from the anastomosis the former was 0.21 mm. and the latter 0.48 mm. At the anastomosis the muscular layer terminated mainly by sending elastic fibers to intermingle with similar fibers of the muscular coat of the artery, the muscle cells gradually disappearing. The fibers of the outer layer formed a dense whorl around the ligature situated at the end of the vein.

The adventitia also appeared to consist of two layers. At a point 1.7 mm. from the anastomosis the inner was 0.45 mm. and the outer ones 0.47 mm. thick, while 11.0 mm. from the anastomosis, they were 1.74 mm. and 0.46 mm. respectively. The outer layer was composed principally of loose connective tissue, which was continuous with the corresponding layer of the artery. The inner layer was continuous with the outer portion of the granular mass lying between the middle and outer coats of the artery, from which it differed markedly in structure, being mainly composed in the vicinity of the anastomosis of dense fibrous tissue containing many elongated nuclei. In addition it received fibers from the inner portion of the outer arterial coat; a few scattered elastic fibers were also present.

The ligatures 0.16 mm. in diameter and three in number were all situated between the middle and the outer coats. One situated in the end of the venous segment near the anastomosis and cut transversely was surrounded by elastic fibers, which were continuous with the fibers of the fibrous layer of the middle coat of the vein. Another cut in a similar manner and situated in the end of the artery was surrounded by fibers similar to the ones surrounding the first and were continuous with the fibers of the muscular layer of the artery. The other ligature was apparently cut through a knot. It was situated between the middle and outer arterial coats and was embedded in the base of the wedge of granular material occupying that situation. It may be that the wide separation of the coats of the vessel and the presence of such a large amount of granular material at this point was partially due to the presence of this knot, as it was quite bulky.

From the microscopic examination it is possible to conclude: (1) The wall of the artery is only slightly altered; (2) the wall of the vein has become enormously thickened, the muscular and fibrous layers of the middle coat and the inner layer of the outer coat being principally involved; (3) no evidence of weakening or breaking down of the wall is observed; and (4) the ligatures are enveloped in a dense coat of fibrous tissue.

CONCLUSIONS. 1. A venous segment interposed between the cut ends of an artery quickly undergoes anatomical changes.

2. From macroscopic and microscopic standpoints the vein has a strong tendency to assume the character of an artery.

3. From a physiological standpoint it performs the arterial functions.

ESSENTIAL PENTOSURIA IN TWO BROTHERS.[1]

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Historical. Salkowski and Jastrowitz, in 1892, first observed the excretion in the urine of an optically inactive sugar which did not ferment with yeast. This they identified as a pentose,[2] by the melting point of its osazon. In 1895, Blumenthal reported two more cases from Salkowski's laboratory. Since that time additional observations have brought the number of indubitable instances of this metabolic anomaly to seventeen, all but a few of which are from Salkowski's laboratory, or the first medical clinic in Berlin. One true case and several questionable ones have come from Italy, and a careful study of two patients from Norway; but no single instance has yet been reported in the British, French, or American literature. The condition is evidently rare, but may frequently have escaped detection or publication.[3]

Apart from its theoretical interest, pentosuria is of importance clinically because of its confusion with diabetes in almost every recorded case—an error which, once the existence of pentosuria is in mind, may be easily avoided.

After a careful study of the original reports the seventeen cases reported by the following observers seem to me unquestionable: Salkowski and Jastrowitz[4] (Case I), Blumenthal[5] (Cases II and III), Bial[6] (Cases IV and V), Meyer[7] (Case VI), Luzzatto[8] (Case VII), Blumenthal[9] (Case VIII), Brat[10] (Cases IX and X), Bendix[11] (Case XI), Bial[12] (Cases XII, XIII, XIV, and XV), and

[1] Read at a meeting of the Association of American Physicians, Washington, D. C., May 15 and 16, 1906.

[2] The pentoses are sugars containing five carbon atoms; the better known grape sugar, fruit sugar, etc., being hexoses with six. The various members of the group differ from one another in the position of attachment of the OH groups, as do dextrose, levulose, and galactose, for instance, among the hexoses. Pentoses are common in the vegetable kingdom, in fruits and stems especially. The most important ones are l-arabinose and l-xylose. In the animal body, pentoses are present in the nucleoproteids, that of the pancreas and of the liver having been identified as l-xylose.

[3] One case I know has been definitely studied by a member of this Association, Prof. E. K. Dunham, though never put on record.

[4] Centralbl. f. d. med. Wissenschaft, 1892, xxx, 337.

[5] Berl. klin. Woch., 1895, xxxii, 567.

[6] Ztschr. f. klin. Med., 1900, xxxix, 473.

[7] Berl. klin. Woch., 1901, xxxviii, 785.

[8] Festschrift f. P. Albertoni, Bologna, 1901; Beiträge z. chem. Physiol. u. Pathol., 1904-5, vi, 87.

[9] Die deutsche Klinik, 1902, No. 71–72, Amer. edit., Modern Clinical Medicine, Diseases of Metabolism, p. 262.

[10] Ztschr. f. klin. Med., 1902, xlvii, 499.

[11] Münch. med. Woch., 1903, liii, 1551.

[12] Berl. klin. Woch., 1904, xli, 552.

Klercker[1] (Cases XVI and XVII). In addition, von Jaksch[2] refers to a case he has had under observation for some time and is about to publish. This with Dunham's unpublished case and my two would make twenty-one cases in all.[3]

The cases of Reale and of Colombini, included by Bendix in his monograph, but with some doubts, I do not think can be admitted as chronic pentosuria, on account of the disappearance of the pentose after a short time. In Reale's case, also, the differentiation from glycuronic acid was not carefully made. Neuberg mentions d'Amato as publishing a case, but this was an example of pentosuria accompanying severe pancreatic diabetes.

In all the above cases except Luzzatto's the pentose was optically inactive; and in one, Neuberg succeeded in isolating the r-arbinose. Luzzatto, in his second paper, described the osazon he obtained as dextrorotary to the same degree as that of l-arabinose. Whether -this is a unique case, with the excretion of l-arabinose alone, or possibly an alimentary pentosuria accompanying the chronic r-arabinose excretion, as has been described, does not seem to me proved.

PERSONAL OBSERVATIONS. The two cases observed by me are a reproduction of those already on record and I report them in brief as showing the usual clinical history.[4]

CASE I.—Male, aged twenty-eight years, married, a salesman. Born in Germany. His father died, aged sixty-two years, of angina pectoris; mother aged thirty-two years, of some liver trouble. The mother suffered from migraine. Three brothers and five sisters are living and healthy, except that one brother has a little "sugar" also.[5]

The patient had tuberculous glands of the neck operated on eight years ago, and catarrhal jaundice at the age of eighteen years, but no other illness. He has never been robust, and has suffered from headaches as long as he can remember. During the period of observation he had a sharp attack of renal colic. He was refused life insurance five months ago because of "sugar," and has been on a rather restricted diet since. Sugar had been found, however, as long as a year ago.

Physical examination was wholly negative.

Urine. 1050 c.c., in twenty-four hours; specific gravity, 1028; highly acid, without albumin, but reducing Fehling's solution, and giving a doubtful bubble in the fermentation tube prepared without

[1] Nord. med. Arch., 1905, xxxviii, abt. ii, S. 1. 55.

[2] Zentralbl. f. innere Med., 1906, xxvii, 145.

[3] Since this paper was read, Blum (Ztschr. f. klin. Med., 1906, lix, 224) has reported two additional cases without family tendency; Kaplan (New York Med. Jour., 1906, lxxxiv, 233) has reported a case of intermittent pentosuria and glycosuria, which, though not true chronic pentosuria, is of much interest; and Johnstone (Edin. Med. Jour., 1906, lxii, 138) has reported a case from von Jaksch's clinic.

[4] I wish to thank my father, Dr. E. G. Janeway, and the family physician, Dr. H. A. Bernstein, for the privilege of studying these patients.

[5] I have not been able to examine the remaining brothers and sisters. One uncle has no pentosuria.

special care as to air bubbles in the urine. This was on a diet containing considerable bread, milk, and fruit.

He was put on a proteid-fat diet, plus 120 grams of toast, to test his tolerance, and the trace of sugar remained unchanged, even after he developed a slight Gerhardt reaction. After a short time the lack of relation between his reported sugar excretion and his diet was so evident that I suspected the presence of pentose, and looked for it. The orcin test was strongly positive, as was the phloroglucin test. Nylander's reagent gave a light-brown color. The reduction of Fehling's solution did not occur for a few minutes after boiling, and then the change of color was sudden to a greenish yellow throughout.

During almost daily observations for two months no positive evidence of fermentation was ever obtained, no rotation of polarized light, and the pentose color and spectroscope reactions were always positive. One hundred grams of dextrose at a single dose failed to produce the slightest glycosuria, as evidenced by fermentation or the polariscope. The phenylhydrazin test was always positive. The osazon was obtained from a large quantity of urine, concentrated *in vacuo*, and its melting point found to be 154 to 158° C. For assistance with this I have to thank Prof. John A. Mandel. The nitrogen content of the osazon has not yet been determined, as all the substance is being used by Prof. Mandel and Dr. Levene, in the attempt to isolate the pure arabinose.

The daily amount of reducing substances excreted was estimated as dextrose, by titration with Pavey's solution—which seems to me rather preferable to Knapp's solution, used by others for this purpose—and found to vary between 2.46 and 4.2 grams, calculated as dextrose.

A study of the effect of diet was made, of a rather unsatisfactory character, because the patient could not control quantities as well as might be desired, but with careful collection of all urine over a long period. The average of the daily estimations by the above method showed the following:

	Average sugar excretion as grams dextrose.
Purin-free diet, 3 days (milk, eggs, rice, toast)	2.56
Ordinary mixed diet, 7 days	3.3
High purin diet, 5 days (much sweetbread, liver and kidney)	3.6
Purin-free diet, 2 days	2.88
Ordinary mixed diet, 2 days	3.1

CASE II.—Brother of Case I, aged twenty-seven years, single, manufacturer. Born in Germany. The patient had meningitis severely at the age of three years; pneumonia as a child, and again three years ago; operations on the nose during the last three years. Has never applied for life insurance. In January of this year he began having headaches like his brother. The urine was examined and sugar found. Restricted his diet for a time only. Correction

of astigmatism cured his headaches. Complained of some palpitation and nervousness, and that he was not very strong.

Physical examination was wholly negative. His urine showed the presence of a non-fermentable optically inactive sugar, giving a typical orcin reaction. The melting point of the osazon was 160 to 162° C. The patient came under observation only a couple of weeks ago, but the amount of urine and of reducing substance, as dextrose, is exactly similar to the other case, from 2.46 grams on a purin-free diet to 3.95 grams on a diet high in nucleins.

I hope to be able in the future to undertake a more complete study of these cases, as well as an investigation of the remaining members of their family.

PRESENT STATE OF OUR KNOWLEDGE OF PENTOSURIA. Three different types of pentosuria have so far been observed, the distinctions between them being important. Alimentary pentosuria, analogous in every way to alimentary glycosuria, occurs whenever large amounts of vegetables or fruits containing pentosanes are eaten, though it is usually very slight. Von Jaksch (*loc. cit.*) has just called attention to its frequency in patients who take much of the pure fruit juices—apple, for instance. Alimentary pentosuria is distinguished, apart from its transitory character and evident cause, by the polariscopic reaction, no optically inactive vegetable pentose being known.

A second group contains those rare cases of severe diabetes in which the inability to burn carbohydrates extends to the pentoses as well as the hexatomic sugars. I have not personally observed this, though on the watch for it during the past winter, but authentic cases like d'Amato's are on record. This group, also, has no real relation to essential pentosuria.

The third group, chronic pentosuria, occurring without reference to the pentoses of the food, and persisting unchanged for years, is a very difficult problem in intermediary metabolism. The definite facts thus far ascertained are as follows:

The sugar excreted is the optically inactive r-arabinose (with the possible exception of Luzzatto's Case VII). This is the only known occurrence of an optically inactive sugar anywhere in nature. It, therefore, cannot be derived from the vegetable pentoses, nor from the l-xylose of the food nucleins. Blumenthal[1] says that he and Bial have found the arabinose in the blood.

The amount excreted is small and fairly uniform in the various cases, from 0.2 to 0.6 per cent., as a rule. Blumenthal's Case VIII, with 1 per cent., is the highest on record. The urine quantity in no case has been excessive. The specific gravity is somewhat increased, and the acidity usually marked.

In a few cases small amounts of glucose have appeared from time

[1] Deutsche Klinik, loc. cit.

to time (Cases I and XVI, possibly IX), but tests with 100 grams of glucose have shown no diminished tolerance for this sugar. In my first case I am unable absolutely to exclude a trace of glucose, in the period before the discovery of pentose, but I consider its presence highly improbable.

The power of burning dextrose has been normal in all the cases examined (Cases IV, XI, XVI, XIX, and my Case I). The tolerance for other carbohydrates has also been tested by Bial[1] and by Klercker,[2] who found levulose, galactose, and, the former, l-arabinose, as fully utilized.

He also found no increase in pentosuria after feeding 500 grams of thymus. Further experiments with inactive galactose are necessary, in the light of Neuberg's theory.

The nuclear metabolism has not been increased, as measured by the excretion of purin bodies and of phosphorus,[3] hence[4] the source of the pentose cannot be an abnormal nuclear destruction, as was to be expected from other considerations.

Klercker, as well as I, have found a diminished pentose excretion on a milk or purin-free diet; Klercker obtained his lowest figures during hunger. He also found a certain parallelism between total nitrogen and pentose in the urine. Blumenthal also states that he and Meyer have found that a meat diet increased the nervous disturbances in these patients, and a milk diet was particularly advantageous. These facts would seem to point toward some relation between the abnormal production of r-arabinose and the activity of metabolic processes.

A family predisposition seems well-marked (Cases IX and X, XI, XII and XIII, XVI and XVII, and my two). The nineteen cases represent only fourteen families, and this question of heredity was not studied with most of the other patients.

The relation to morphine and cocaine addiction, at first supposed, because of Salkowski's original case, has not been substantiated. Reale's and Colombini's patients were of this character, but were not true chronic pentosurics.

In many of the cases neurasthenic symptoms and neuralgic pains have been prominent. Others have been perfectly well when once freed from the restrictions of a diabetic regimen.

Concerning the real nature of the malady, we can only say that it is an anomaly in the intermediary metabolism, rather analogous to cystinuria and alkaptonuria than to diabetes.

DIAGNOSIS. The recognition of new cases of pentosuria must depend largely upon clinicians, who should be conversant with the simple tests necessary to establish the diagnosis as a probability.

[1] Verhandl. d. XIX Cong. f. in. Med., 1901, p. 413.
[2] Nord. med. Arch., 1905, xxxviii, Abt. II, p. 1 and 55.
[3] Die Pentosuria, Stuttgart, 1903, p. 49.
[4] Loc. cit.

Any urine which reduces Fehling's solution in an atypical way, the color remaining unchanged for a minute or so after boiling and then suddenly turning a greenish yellow or muddy orange throughout, should be subjected to further tests. If it yield good crystals with the ordinary phenylhydrazin test, does not ferment with yeast, and is optically inactive, pentose is probably present.

The orcin test, with the precautions urged by Brat,[1] should be used, whenever there is any suspicion. To 3 c.c. of urine add 5 c.c. of concentrated HCl, specific gravity 1.19, and a knife-point-full of orcin. With a thermometer in the test-tube, heat on a water-bath at 90 to 95° C for two or three minutes. In the presence of pentose a green precipitate will form, which should be taken up with amyl alcohol and examined spectroscopically, an absorption band in the orange and contiguous red being typical of pentose. Too prolonged heating may split up the conjugate glycuronic acids, which will then give the reaction, and are the only possible sources of confusion. (Menthol and turpentine glycuronic acids break up spontaneously, but may be recognized at once by their odor.) Heating over the direct flame may fail to produce the typical reaction when pentose is present; but, if the other method is impossible, may be resorted to for ruling out pentosuria. I have also found that very concentrated urines often give a gummy red precipitate, which obscures the green, and these should be diluted one-half.

When the orcin test is positive[2] [3] the absolute proof must be sought in the preparation of the osazon, with phenylhydrazin. If the melting point of this be found about 156 to 160° C., and its N. content about 17.07 per cent., then the diagnosis is beyond question. This must, of course, be left to a competent chemist.

Clinical Significance of Essential Pentosuria. No patient with pentosuria has been under surveillance a sufficient length of time to speak with absolute certainty of its course or prognosis. No bad results have yet been noted, though Blumenthal considers it possible that the increase in circulating sugar may conduce to arteriosclerosis, as in diabetes. There is, of course, no loss of an important foodstuff, as in the latter disease, and the prognosis is certainly better than in the mildest diabetes. In life insurance, I think this should be the attitude toward such cases. It is in life insurance examining that the condition should be most often found, and it is a gross injustice to class these people with diabetics.

The only treatment consists in carefully explaining to the patient the difference between his ailment and diabetes, and the removal of any previous dietetic restrictions he may have been subjected to.

[1] Ztschr. f. klin. Med., 1902, xlvii, p. 499.

[2] For the differential diagnosis of the various carbohydrates of the urine, see F. C. Wood, Chemical and Microscopic Diagnosis, 1905, New York, p. 548, or F. Blumenthal, Pathologie des Harnes, 1903, p 112.

[3] Otori, Ztschr. f. Heilkunde, 1904, xxv, p. 12, found that he could detect the presence of arabinose by this method in dilution as low as 0.05 per cent.

LITERATURE.

The full literature of the subject with excellent critical reviews may be found in the following publications:

Bendix, E. Die Pentosurie, Stuttgart, 1903.

Neuberg, Carl. Die Physiologie der Pentosen and Glukuronsaüre Ergeb. d. Physiol., 1904, iii, p. 373.

Klercker, K. O. Studien über die Pentosurie, Nord. med. Arch., 1905, xxxviii, Abt. ii, p. 1 and 55.

The best clinical article is that on Pentosuria by F. Blumenthal, Modern Clinical Medicine, Diseases of Metabolism, 1906, p. 262.

THE VALUE OF MASSIVE DOSES OF THE SALICYLATES IN THE DIAGNOSIS AND TREATMENT OF ACUTE ARTICULAR RHEUMATISM.

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For the last six years, in the treatment of acute articular rheumatism at the Lakeside Hospital, the tendency has been to a progressive increase in the dosage of sodium salicylate employed. Beginning with ten grains every two hours or fifteen grains every four hours, the amount used has been increased to ten grains, fifteen grains, or even twenty grains hourly in the endeavor to secure the drug effect as promptly as possible. This massive salicylate dosage has seemingly been of such value in the prompt and sure control of symptoms that an analysis of the hospital cases so treated has been undertaken in a critical review of the question. In the review it has seemed only fair, in order, if possible, to learn the exact effect of these large doses, to exclude certain classes of cases. For this reason, all patients who showed an acute complication on admission to the hospital and those in whom, on admission, the temperature was normal, probably due to medication at their homes, have been omitted. Children below twelve years of age have also been excluded on account of the difficulty of classifying these according to dosage. All other cases are included in the analysis.

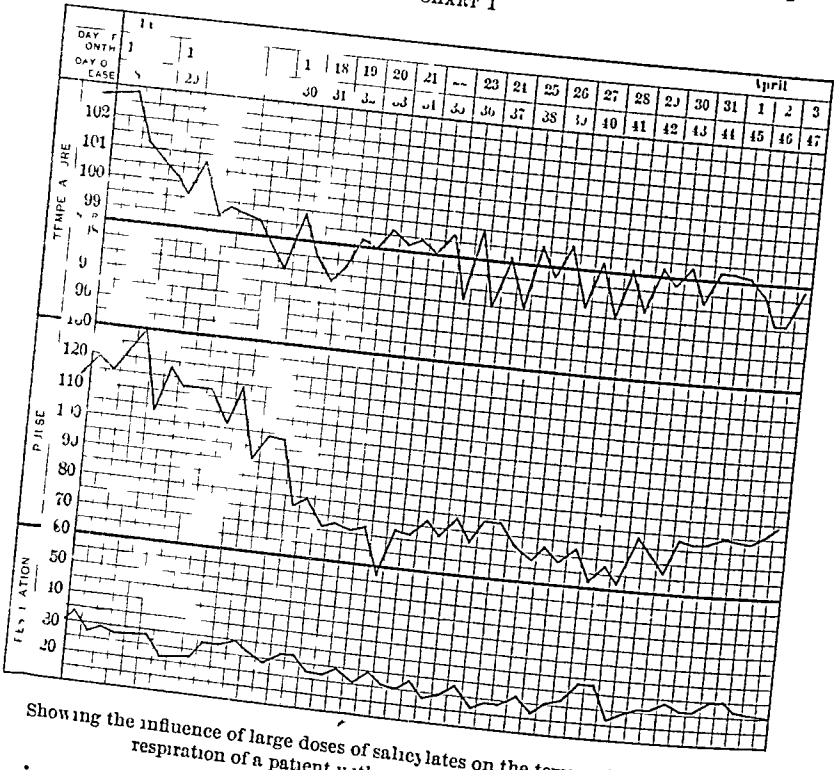
These exclusions leave seventy-four cases of adults admitted with joints acutely inflamed and temperatures elevated. The discussion of the effects of the large doses of the salicylate, an administration of 240 grains, or more, in the twenty-four hours being considered a large dose, will be divided into two heads, therapeutic and diagnostic.

Therapeutic Effects. The routine method of treatment has consisted of giving the sodium salicylate every hour, if the patient was awake, in doses varying from 10 to 20 grains, until the toxic symptoms appeared, the attendants being alert to recognize the appearance of deafness and tinnitus, as an index of full drug effect; the salicylate was then stopped, to be resumed when the symptoms

disappeared, and then given in doses of 10 or 20 grains every two to four hours, stopping again with each recurrence of toxic symptoms. The amount of salicylate required to produce symptoms of its full effect has varied from 75 to 360 grains, the average in the entire series being 200 grains. These massive doses are borne well, as a rule, without nausea, vomiting, or depression, and the coincident relief of pain makes what discomforts there are seem trivial.

Fever. The effect of this sudden saturation with the drug is a very rapid fall of the temperature to the normal. Chart 1 of a patient who became toxic on 165 grains shows this fall very typically.

CHART 1



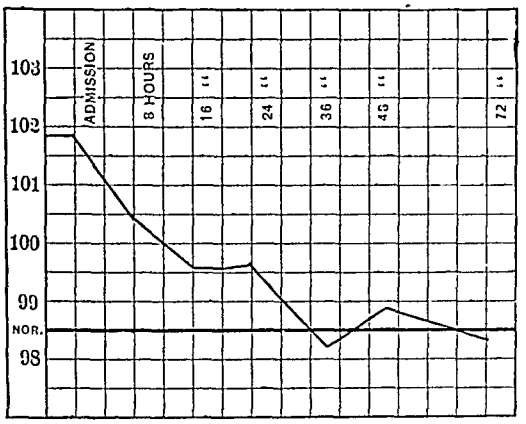
Showing the influence of large doses of salicylates on the temperature, pulse, and respiration of a patient with acute articular rheumatism

Coming in with a fever of 102.8° F. at 8 P.M., in twenty-four hours the temperature was 99°, and in thirty-six hours it was subnormal. That this is not exceptional, and is, in fact, what is expected under this treatment, is shown by Chart 2, which is a composite of the temperature of the first three days of the entire series of seventy-four patients. A study of the number of days of fever after the patient's admission shows that the shortest period was one day and the longest eleven days, with an average fever of 3.8 days. The average febrile period of the illness, including the time before treatment was begun, while the patient was still at his home, was thirteen days.

Pain. The relief from pain is most striking. A patient brought in during the afternoon, in such acute agony that a touch of the bedclothes or a jar of the bed causes a cry of anguish, and who may have required a dose of morphine to allow the nurse to remove his clothing, frequently greets the physician with a smile the following morning at the ward visit, and often moves his joints himself to show his improvement. The pain in some patients is entirely absent on the second day and never returns. Our analysis of the seventy-four cases shows that by the fourth day the average patient is free of discomfort. The longest period of pain has been nine days.

Swelling. The swelling rapidly subsides, sometimes before the pain, and sometimes persists in a mild degree for a day or two longer. The records upon this point have not been as full as might be desired, but of cases in which the note was made, the swelling disappeared, on the average, on the third day after admission. In

CHART 2



A composite of the temperature of the first three days of seventy-four patients with acute articular rheumatism, showing the influence of large doses of salicylate.

but four of the seventy-four patients has any joint become involved after the treatment was begun.

Heart. Owing to the general belief in the danger to the heart of using the salicylate in large doses this organ has been watched with especial care, and it has been gratifying to see in how few of our cases this fear has been justified. Cardiac complications instead of being increased in frequency by this method of treatment seem to be lessened. The prevalence of acute endocarditis occurring during rheumatism is given by various authors at different rates. W. Gilman Thompson[1] gives acute endocarditis as occurring in 25 per cent. of the cases; Anders[2] in from 25 to 30 per cent. Polton[3] quotes the following authors: Bamberger, 20 per cent.; Wunderlich,

[1] Amer. Syst. Prac. Med., vol. iv, p. 958.
[2] Practice of Medicine, Phila., 1898, 2d ed. p. 206.
[3] Jour. Amer. Med. Assoc., 1903, xl, p. 83.

9 per cent.; Bellevue Hospital reports, 33 per cent.; Anders, 40 per cent.; and West, 61.3 per cent. A study of McCrae's recent articles[1] shows that of 153 patients in whom the heart was clear on admission, 48 at some time developed some sign of cardiac complication, a percentage of 31, which just agrees with the average of those above mentioned. In our series of 74 patients, 46 had apparently normal hearts on admission to the hospital, and of these, only 6 developed any sign of an endocardial complication. In 4 of these the murmur persisted at discharge, and in 2 it was only temporary and disappeared under observation. This record of 13 per cent. of endocardial complications certainly compares favorably with general experience. There was 1 case of pericarditis in our series of 74 cases. During this period there were several other cases of rheumatic pericarditis in the hospital, but as they were admitted with the complication, they could not be included in this series.

In most of our cases the alkalies in the form of potassium acetate and citrate were given. In eighteen of the cases, however, it was omitted and dependence was put upon the salicylate alone. Though the numbers are too small for conclusions to be drawn, it is of sufficient interest to note in passing that all the six cases of cardiac complications occurred in the patients who received alkalies, and none in the fourteen patients with normal hearts on admission, who were on the salicylate alone.

The depression of the heart, so often spoken of in connection with salicylate treatment, has not been evident in our cases. The pulse usually drops within three days to from 70 to 80, as is shown in Chart 1, and remains at that level, strong and regular during convalescence. In one case only in which there was no evident endocarditis has the pulse weakened. In this case it rose to 120 and remained elevated for three days, when it again returned to the normal rate and no further trouble was experienced.

Danger. In the use of such large doses of sodium salicylate there is a certain element of danger. With proper care and attention, however, this is not great. The toxic symptoms must be watched for carefully, and their appearance indicates the immediate stopping of the drug. Again, too, as some persons show no toxic symptoms until they have taken enormous quantities, it would be well to put a limit upon the amount to be given. In the only fatal case in our series the patient took, without any signs of poisoning, 580 grains, at the rate of 20 grains an hour. At this point we discontinued the drug and for two days he did well; then he suddenly became wildly delirious and developed retraction of the head, Kernig's sign, and a high temperature. A lumbar puncture brought out clear fluid under pressure, which showed nothing

[1] Jour. Amer. Med. Assoc., 1903, xl p. 211; American Medicine, 1903, vi, p. 221.

abnormal on examination. The condition continued and progressed until the patient died on the tenth day. The autopsy showed marked œdema of the brain, or serous meningitis, and vegetative endocarditis. We are loth to attribute this man's death to salicylate poisoning, and think it was more likely a case of rheumatic meningitis. The possibility however, must be considered of the drug having caused the symptoms.

The main objection to the use of the massive doses is the difficulty in keeping the patients at rest after the first three days. Feeling comfortable, and, as they express it, cured, most of the unintelligent public ward patients can see no reason for remaining in bed, and clamor to go to their homes to work, and it is often hard or impossible to keep them on their backs for the three weeks after the last symptoms have disappeared, a procedure which has seemed advisable.

Diagnosis. More and more attention is being paid each year to the diagnosis of the various forms of arthritis, particularly to the differentiation of the real cases of rheumatic fever from other infectious forms of arthritis, and especially from the acute stage of arthritis deformans, the latter of particular interest since McCrae's[1] article on the subject appeared in 1904. With this point in view the series of cases here reported has been watched, and the impression has steadily gained strength that in using the salicylates in these large doses, they are of value as a diagnostic test. The amount of the drug which a patient will take before becoming toxic is the first point to be considered, and it has constantly been observed that whereas the true rheumatic can tolerate from 150 to 300 grains before symptoms appear, persons suffering from other forms of arthritis become toxic on much smaller doses, the gonococcic cases for example averaging in our series 131 grains. The second point is the relief from symptoms. In true rheumatism the fever, pain, and swelling are gone in from two to three days. In the other forms of arthritis, while the antipyretic effect of the drug may bring the temperature to normal, and while the depressed sensorium may not appreciate the pain so acutely, the swelling does not go down and, as soon as the toxic effects of the salicylate wear off, the pain returns with all its old vigor. The result of this has been that, on this service, any patient having fever and pain at the end of forty-eight hours is considered as a doubtful case of rheumatism and most careful search is instituted for the underlying cause of the arthritis. A *resume* of the cases of gonorrheal arthritis to which the massive doses were given, during recent years, shows by contrast to the above an average run of fever of twenty-one days after admission, of pain of twenty-six days, and of swelling of thirty-one days. These numbers should really be larger

[1] [illegible] Vol. [illegible], 1904, No. [illegible], p. 8, 91, and 361.

than this shows, as in many cases the date used is that on which the patient was transferred to the surgeons before improvement had begun. An attempt to review the cases of typhoid and other infectious arthritis, of arthritis deformans, tuberculous joints, and gout showed so few cases treated with massive doses of salicylates that they could not be used in comparison.

I was especially impressed with this point in analyzing the histories for this report by finding one case which differed most materially from the others. The history, taken in 1901, was of a man admitted with acute polyarthritis, who, although he received 15 grains of the sodium salicylate every hour did not respond to treatment in the uniform manner of the other cases of the series. It was a typical case of rheumatism and was so diagnosed at the time. On re-reading the history to find an explanation for the failure of response to the drug, the patient's name being noticed for the first time; it was recognized as that of a patient at that time, four years later, in the ward with the typical chronic spondylitis and dactylitis of arthritis deformans.

CONCLUSIONS. 1. Sodium salicylate can and should be given in much larger doses than are generally used.

2. Given in massive doses it reduces the fever, relieves the pain and swelling, and shortens the course of the disease.

3. It is not injurious to the heart, and appears by quickly cutting off the disease to offer some protection to that organ.

4. The patient's tolerance to the drug and the rapid cessation of symptoms form valuable therapeutic tests for the diagnosis of acute articular rheumatism.

For permission to use the cases from the medical service, I wish to thank Drs. Hunter Powell, John H. Lowman, Henry Upson, and Edward F. Cushing, visiting physicians to the Hospital and especially Dr. Cushing, for many suggestions and ideas, here used, and for oversight and criticism of the work during preparation.

Since writing this article my attention has been called to the Harveian Lecture of Dr. Lees,[1] who has made a careful study of the use of massive doses of salicylates in rheumatism.

[1] The Treatment of Acute Visceral Inflammations, London, 1904.

A NEW BLOOD FILARIA OF MAN: FILARIA PHILIPPINENSIS.[1]

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AND
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(CONSTITUTING THE U. S. ARMY BOARD FOR THE STUDY OF TROPICAL DISEASES IN THE PHILIPPINE ISLANDS.)

Introduction. *Filaria philippinensis* is a small sheathed filaria found in the blood of a Visayan prisoner in Bilibid prison, Manila, at all hours of the day and night, but always in small numbers. At the time of our observations it seemed rather more numerous at night, though even then, it was, at times, hard to find. The greatest number we have found in one slide was seven. Once we examined seventeen spreads and found but one parasite. This was one day at noon. On another occasion a slide taken at noon showed five organisms.

There is a history that the worm formerly occurred in the peripheral blood only in the daytime, when it was found in great numbers, and the hospital records show a diagnosis of *Filaria diurna*. As, according to Manson and other authorities, the periodicity of *Filaria diurna* never changes, and as this worm is now found in the peripheral blood throughout the twenty-four hours, it is obvious that the diagnosis of *Filaria diurna* was erroneous.

We are of the opinion that this filaria represents a new species for the reasons given in the detailed description of the worm, because of its lack of periodicity, and because of the rarity of filariasis in the Philippine Islands, where all the conditions would seem favorable to the rapid spread of infection were the parasite any of the previously known varieties.

While other cases have doubtless been observed in these Islands we are unable to find in the literature more than ten reported cases (all described as *F. nocturna* or *F. diurna*), although many observers have carefully sought for filaria and thousands of routine blood examinations have been and are being made throughout the Islands.

Although in the reported cases the filariæ were diagnosed as *F. nocturna* or *F. diurna*, there is nothing in the descriptions given which excludes the possibility that the observers might have been dealing with *F. philippinensis*, and that the latter is the only filaria indigenous to the Philippine Islands.

Description of Filaria philippinensis, nov. sp. (Ashburn and Craig). Only the embryonic stage of this filaria has been observed.

[1] Published by permission of the Surgeon-General, U. S. Army. Received for publication June 23, 1906.

Length. The average length of the fresh specimen is 0.32 mm Satisfactory measurements are very hard to obtain, as the worm when alive, is constantly in motion, and we cannot be sure that the dead worm, even immediately after death, is of the same length as the living one. There is considerable variation in the length of the living worm, as is shown by the following measurements of twenty specimens.

No. 1	0 325 mm.	No. 11	0.322 mm.
No 2	0 33 "	No. 12	0.292 "
No 3	0 30 "	No. 13	0.315 "
No 4	0 315 "	No. 14	0.310 "
No. 5	0 335 "	No. 15	0.325 "
No 6	0 34 "	No. 16	0.300 "
No. 7	0.326 "	No. 17	0.315 "
No. 8	0.315 "	No. 18	0.310 "
No. 9	0 307 "	No. 19	0.335 "
No.10	0.307 "	No. 20	0.330 "

Stained Specimens. In specimens stained in dilute carbol-fuchsin, after dissolving the hemoglobin of the red cells in distilled water, the worm appears slightly shortened, the average length being 0.296 mm. We have found this stain the most efficient of any we have tried, as it colors the nuclear bodies and brings out the structure of the filaria. Hemotoxylin is almost useless in staining this filaria and Wright's stain greatly shrinks the organism.

Diameter. The average diameter of the worm is 0.0065 mm., a trifle less than the diameter of a red blood cell.

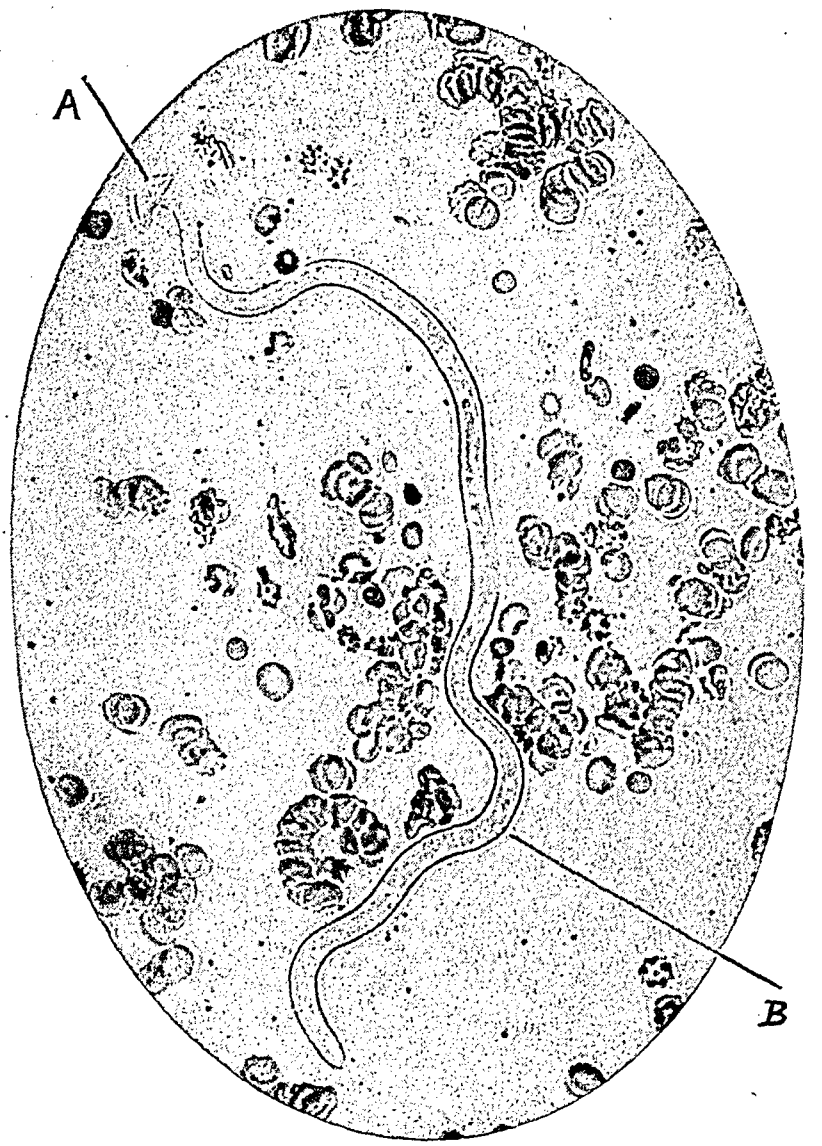
Sheath. This filaria is enclosed within a very delicate, and, in the living specimen, tightly fitting sheath. In the living worm this sheath is very closely applied to the body and can be seen only as a fine thread, resembling a flagellum, at the ends (Fig. 1, *A*), and never distended or flat, as is that of *F. nocturna* or *F. diurna.* The thread-like extremities of the sheath are quite as delicate as the flagellum of a trypanosome, and are lashed rapidly about as the worm moves. The filaria cannot be seen to move backward or forward within the sheath. Under certain conditions to be described later, the sheath may be observed to be separate from the body and distended, especially at the tail end. In stained specimens the sheath is sometimes observed faintly colored and flattened like a band, considerably longer and broader than the worm. The majority of stained specimens, however, do not show the sheath.

Head. The anterior extremity consists of a smooth, hemispherical head, on which is mounted, and into which retracts, a very minute spicule. This spicule when magnified 1800 diameters looks about the size of a very small but oblong eosinophilic granule.

Surrounding this smooth hemispherical head, and when closed, covering it, when retracted, exposing it, is a prepuce, which apparently consists of a musculocutaneous layer very finely serrated at its margin; we have found it impossible to determine the number of serrations or lips on account of their minute size. The prepuce

is constantly drawn back and forth, covering and uncovering the head and spicule, but its motion is not always synchronous with that of the spicule, being usually slower. The appearances described can only be made out as the motion of the filaria ceases, and never in the stained specimens.

FIG. 1



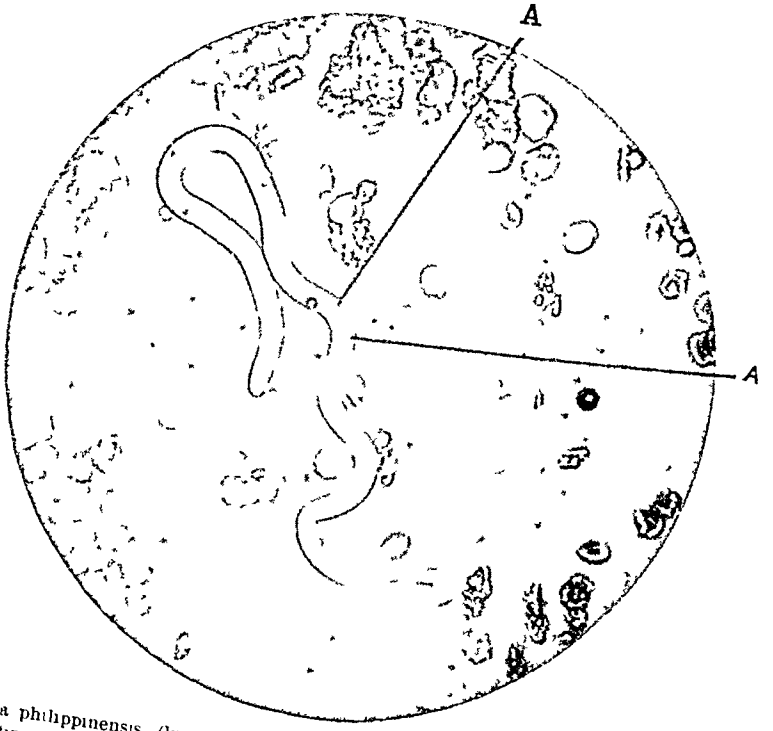
Filaria philippinensis (living organism), showing the anterior V-spot at *B* and the flagellum-like end of the sheath at *A*. (Zeiss objective DD, projection ocular No. 4.)

Body. The body is long, graceful, and sinuous, consisting of an outer or musculocutaneous coat, and an inner portion or body cavity. Under high magnification and in some photomicrographs, a delicate but distinct radial striation can be seen in the musculocutaneous layer (Fig. 4). In the very fresh specimens the inner portion or body cavity is for the greater part clear and highly refrac-

tile, though it contains a few scattered granules and the following constant viscera:

Anterior V-spot. In the posterior portion of the anterior third of the worm is situated the anterior V-spot (Fig. 1, *B*). This is a bright, refractile, triangular spot, placed at one side of the worm and opening by its apex upon the surface. It is situated in the majority of cases about 0.105 mm. from the margin of the head. With high powers the apex can be seen opening between the striations of the musculocutaneous coat, evidently piercing it. This

FIG 2



Filaria philippinensis (living organism) showing the central or "spiral" viscus at *A*. The entire spiral is not in focus, only the top of the loops being visible (Zeiss objective DD, projection ocular No 4)

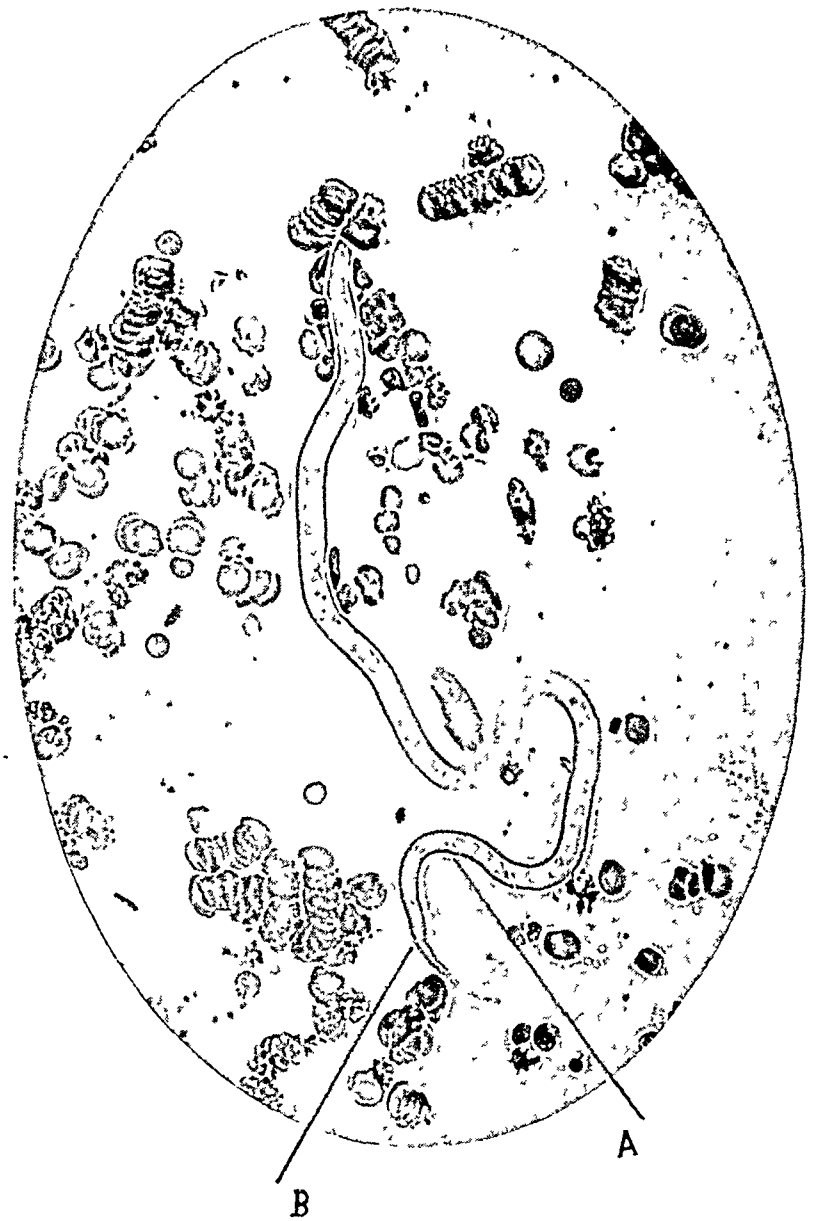
spot has not been observed to show contractility. In stained specimens the anterior V-spot cannot be seen.

Central Viscus. In the central third of the body of the filaria, usually towards the posterior end of it, but at times pushed forward, is the central viscus, which for *F. nocturna* and *diurna* is described by Manson as "a granular mass," but which in this filaria is clearly and easily seen to be a convoluted or spiral tube or cylinder, resembling much a vine tendril, and showing five or six spiral turns (Fig. 2, *A*). (Note: In the photomicrograph only the portion

of the spiral turns in focus are shown.) Its tubal diameter is about 1 micron, its spiral diameter about 2 microns or a little more.

The spiral organ is only observed in fresh and undegenerating specimens of the filaria.

FIG. 3



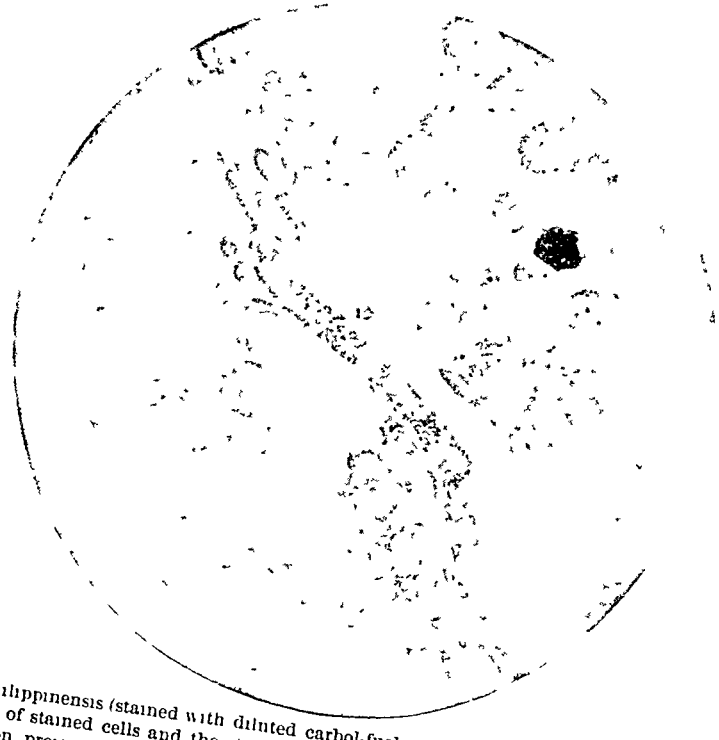
Filaria philippinensis (living organism), showing the anal papilla at *A*, and the sudden attenuation of the tail at *B*. (Zeiss objective DD, projection ocular No. 4.)

Posterior V-spot and Papilla. At about the middle of the posterior of the worm are situated the posterior V-spot and the papilla. The V-spot cannot always be seen as easily as the anterior V-spot, but in the vast majority of cases it can. It is placed with the apex opening upon the surface, breaking or piercing the musculocutan-

eous coat. In addition to the appearances presented by the anterior V-spot, this one marks the site of a distinct papilla which bulges beyond the general body line (Fig. 3, *A*). (Note: The papilla is in focus, but not the V-spot.) This point may represent the anus or cloaca of the adult worm; at any rate it is a point of minor resistance in the embryo, as shown by the following phenomena which may at times be observed:

If spreads of fresh blood be made, and not "ringed," a negative pressure will sometimes develop under the cover-glass, as the blood dries. In such instances the worm, if it be kept in the field of a

FIG. 4



Filaria philippinensis (stained with diluted carbol-fuchsin), showing the anterior "gap" in the column of stained cells and the striation of the musculocutaneous coat. (Zeiss 1/12 inch oil immersion, projection ocular No. 4.)

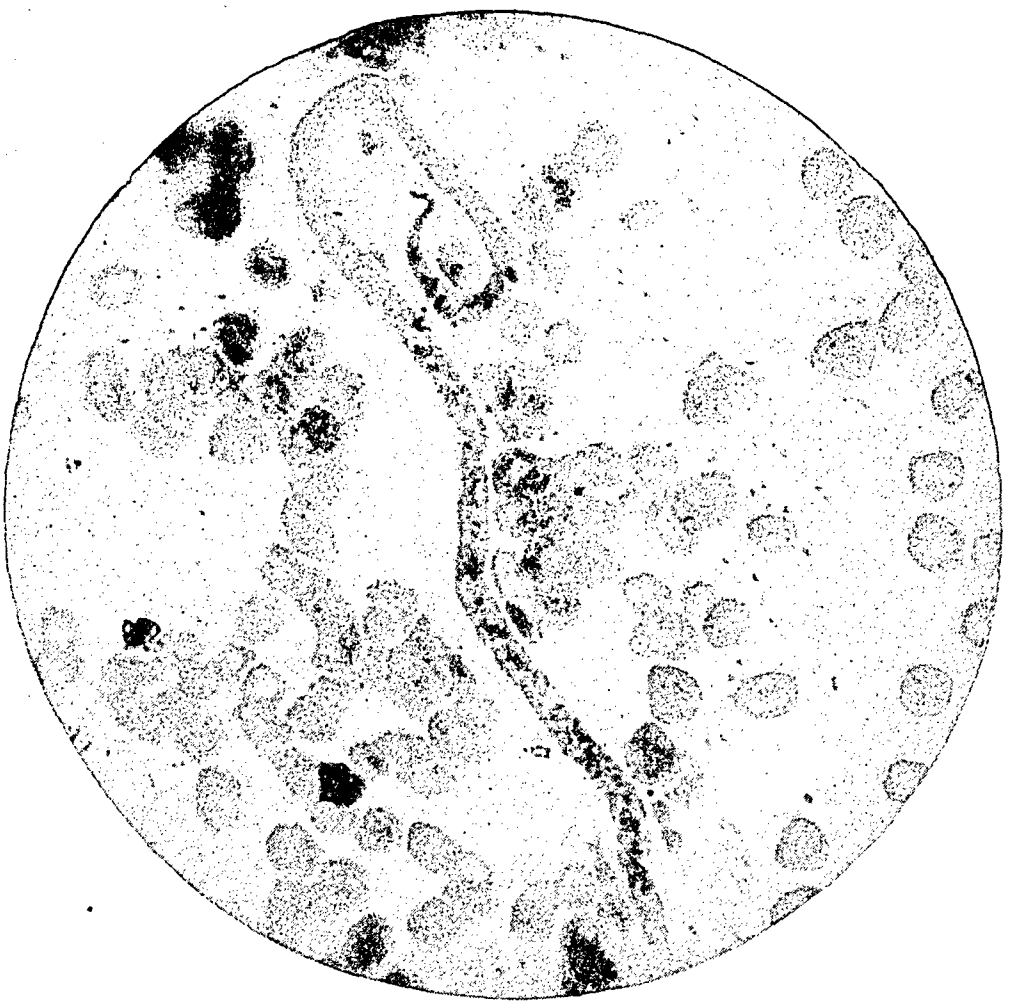
one-twelfth inch objective, will appear too small and the anal papilla will become prominent. Soon it will evert and the V-spot will be inverted and upon the outside of the body, though still attached. Finally, the V-ruptures and fluid, or gas, or both, containing granules, flows out of the body of the filaria and between it and the sheath, distending the latter and separating it from the body. Degenerative changes then follow rapidly, the central viscus, the V-spot, and later, the striations of the musculocutaneous layer disappear, and the body cavity becomes filled with vacuoles and granular material.

In stained specimens the posterior V-spot is not visible.

Tail. Midway between the posterior V-spot and the tip, the tail suddenly becomes attenuated to three-fourths its former diameter, making a distinct offset on each side. From this offset it diminishes progressively and uniformly to a very fine point (Fig. 3, *B*).

The relative position of the embryonic anus and the apparently less vital character of the small portion of the tail beyond the atten-

FIG. 5



Filaria philippinensis (stained with diluted carbol-fuchsin), showing the column of stained cells, the anterior "gap," and the sudden attenuation of the tail. (Zeiss objective DD, projection ocular No. 4.)

uation, suggests that during development of the worm this portion of the tail dies or is sloughed off at the point of diminution.

Stained Specimens. In stained specimens a column of deeply colored spots, round or oval in shape, is observed running the entire length of the worm, but broken, here and there, by unstained areas, which vary in situation in individual specimens. The stained spots are apparently the nuclei of the body cells. There is a clear,

unstained space between the column of nuclei and the outer border of the filaria, on each side.

In view of the fact that Daniels, Dutton, Annett, and others, state that the position of unstained "gaps" in the column of stained spots in filaria are of diagnostic value in the differentiation of species, we have carefully stained many specimens of our filaria, but have not found that in this organism much reliance can be placed upon the situation of the "gaps," since they vary markedly in position in individual filaria.

The only interruption or "gap" in the column of stained granules in *Filaria philippinensis* which can be said to be at all constant is the "gap" situated anteriorly, at a point about 20 per cent. of the total length of the worm from the margin of the head (Figs. 4 and 5). Many specimens do not show this "gap," however, and upon reference to the following table it will be seen that there is much variation in the situation of this "gap" in individual worms. The table also shows the variation in length of the worms in fuchsin stained specimens.

No.	Length of stained worm.	Anterior "gap" in percentage of total length.
1	0.325 mm.	23
2	0.29 "	19
3	0.28 "	23
4	0.285 "	22
5	0.315 "	22
6	0.31 "	21
7	0.315 "	17
8	0.33 "	22
9	0.31 "	19
10	0.30 "	20
11	0.29 "	22
12	0.285 "	18
13	0.255 "	20
14	0.25 "	18
15	0 32 "	Anterior "gap not apparent
16	0.30 "	
17	0.315 "	
18	0.295 "	
19	0.30 "	
20	0.30 "	
21	0.30 "	
22	0.285 "	
23	0.28 "	
24	0.30 "	
25	0.285 "	

In a few stained specimens a loose arrangement of the stained nuclei may be observed in the region of the spiral viscus, and a break near the posterior V-spot, but neither of these is of any diagnostic importance, as they occur comparatively seldom, and other worms show a similar arrangement of the stained nuclei in very diverse situations.

A very constant arrangement of the stained nuclei in the tail is in the form of a single row of rod-shaped or slightly oval spots, which become smaller and smaller as the tip of the tail is approached.

Motility. This filaria is very active in its movements, wriggling about so rapidly that it cannot be well studied for some hours after the blood is drawn. The motion, in most instances, is not progressive, but at times it is markedly so. Motion continues in "ringed" preparations and at room temperature, when the thermometer shows a maximum of 98° F., and a minumum of 80° F., for about thirty-six hours in hardy individuals.

Our attention has been called by Dr. Martin, the Government photographer, to the fact that our filaria is more resistant to the action of the arc light, during the taking of photomicrographs, than is *Filaria nocturna.*

Degenerative Forms. Very marked degenerative changes occur in this filaria and no safe conclusions can be drawn regarding its morphology after degeneration has once begun. The anterior V-spot, the spiral viscus, and the posterior V-spot and papilla disappear, and the entire organism becomes filled with granular material and vacuoles. The morphology of this organism can only be well studied in the fresh specimen.

Pathogenicity. Having observed but one case of infection with this filaria, we are not, at present, prepared to say what symptoms may be produced by it. This one patient has had several attacks of chyluria, though not during the period of our observations. He has no markedly enlarged glands, no lymphatic varices, no elephantiasis that we can detect. His skin is dry and rough and his general appearance one of rather poor nutrition, but these conditions may be quite as readily accounted for by his imprisonment as by the filariasis.

CONCLUSION. In conclusion, the following table is appended, giving the chief differential points in the structure of the previously described filariæ and *Filaria philippinensis.*

Name	Length	Breadth	Sheath	Head	Tail	Ant. V-spot	Viscus	Post. V-spot	Motility	Periodicity
F. nocturna.	mm. 0.30	mm. 0.0075	Present Loose	6 lips	Pointed	Present	Granular mass	Present	Lashing not progressive	Nocturnal
F. diurna	0.30	0.0075	Present Loose	6 lips	Pointed	Present	Granular mass	Present	Lashing not progressive	Diurna
F. perstans.	0.20-0.23	0.0045	Absent	Papillated	Blunt	Negative	Negative	Negative	Lashing and progressive	None
F. demarquai.	0.20	0.005	Absent	Spine	Pointed	Present	?	?	Progressive	None
F. ozzardi.	0.21	0.005	Absent	?	Pointed	?	?	?	Progr's-sive?	None
F. philippinensis.	0.32	0.0065	Present Tight	Serrat. retractile band	Pointed abruptly attenu't'd	Present	A spiral tube or cylinder	Present Also a papilla	Lashing and progressive	None

SPLENOMEDULLARY PSEUDOLEUKEMIA, WITH SECONDARY MYELOPHTHISIC ANEMIA.

By Charles E. Simon, M.D.,
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The patient is a male, aged seventy-nine years, who was admitted to the surgical service of the Maryland General Hospital, March 16, 1906, with a burn of the left hand. He had had the usual diseases of childhood, and typhoid fever at an early age. Otherwise his health had always been good and he had been able to work at his trade as a painter up to Christmas, 1905. He admits that for about a year he has readily become short of breath and that his eyelids have been puffed; his strength, however, has remained unimpaired. He denies venereal disease. Of his thirteen children, all but three have died in infancy. He has never had any lead palsy, but speaks of attacks of colic, which have occurred now and then. There is no malarial history. His digestive functions are good and there has been no material loss of flesh.

The patient is a man of small stature, rather younger looking than his age would suggest. He is fairly well nourished, with good abdominal panniculus, but quite pale, without any lemon tint. Examination of the chest reveals nothing abnormal beyond a blowing systolic murmur heard over the entire precordium, but not propagated beyond the anterior axillary line; the heart dulness is within normal limits. The lymph glands are nowhere enlarged. The abdomen is moderately full. The spleen extends well into the left iliac fossa and forward to within two finger breadths of the umbilicus; the notch is readily felt. The organ is somewhat movable, smooth and fairly hard. The liver is palpable at the right costal border. Percussion of the bones elicits no tenderness. The urine contains a moderate number of granular casts and a trace of albumin.

Examination of the blood showed a very interesting condition. The red cells numbered 2,195,000; the hemoglobin was 25 per cent; the color index was 0.58. While there was a certain amount of variation in size and form of the red cells, there was no manifest tendency to macrocytosis or oval form; true poikilocytes were not numerous. The cells were pale and showed no evidence of polychromasia, while granule cells were present in fair numbers. Nucleated red cells were not found. The leukocytes numbered 22,000. The differential count showed: lymphocytes, 92.6 per cent (of which 2 per cent. large lymphocytes); large mononuclears, 1.6 per cent.; polynuclear neutrophiles, 5.6 per cent.; mast cells, 0.6 per cent.

During the patient's stay in the hospital two other examinations

were made. The findings, so far as the red cells go, were essentially the same as at the time of the first examination, and there were no nucleated red cells. The leukocytes were 10,900 on April 10, and somewhat lower on April 19. The differential counts follow:

April 10th. Lymphocytes, 81.8 per cent.; large mononuclears, 3.0 per cent.; polynuclear neutrophiles, 15.2 per cent.; eosinophiles, 0.0 per cent.; mast cells, 0.0 per cent.; myelocytes, 0.0 per cent.

April 19th. Lymphocytes, 94.5 per cent.; large mononuclears, 1.0 per cent.; polynuclear neutrophiles, 3.0 per cent.; eosinophiles, 1.0 per cent.; mast cells, 0.5 per cent.; myelocytes, 0.0 per cent.

The patient remained at the hospital for observation until April 19th, and died suddenly about a week after returning to his home. Unfortunately no autopsy was obtained.

The clinical diagnosis of the case presented a number of interesting questions. My first impression was that we were dealing with an example of the type of leukanemia described by Leube, in which the blood picture of pernicious anemia is associated with that of leukemia. While in the majority of the recorded cases the leukocytic formula has shown a predominance of granulocytes, lymphocytosis has been noted in others (Körmöczi, Luce, Parkes Weber). In all the recorded cases, however, normoblasts and megaloblasts have been observed, while in my case no nucleated red cells could be demonstrated. I have pointed out, moreover, that the color index was low and that there was no well-defined tendency toward macrocytosis or oval form, as we see it in typical cases of pernicious anemia. It, therefore, did not seem warrantable to classify the case as one of leukanemia, in accordance with the original definition of the term by Leube.

Splenic anemia, in the sense in which Osler uses the term, seemed excluded. There had been no hematemesis at any time and no pigmentation of the skin. The corpuscular anemia was much more marked than is usual in splenic anemia; there was no leukopenia and the leukocytic formula was markedly altered; while in splenic anemia the differential count is not characteristic.

A simple chronic lymphatic leukemia was out of the question in view of the absence of any enlargement of the lymph glands, and against the diagnosis of acute myelogenic lymphoid leukemia, there was the duration of the disease, the practical absence of any clinical symptoms, the splenomegaly, and the predominance of the small lymphocyte in the blood.

Under the circumstances I have ventured to offer the pathologico-anatomical diagnosis expressed in the heading of the paper, as furnishing the most probable explanation of the clinical findings. I am thus inclined to view the splenomegaly as a primary splenic pseudoleukemia and the anemia as the expression of a myelophthisis with substitution of the erythroblastic by lymphadenoid tissue.

INFECTIONS OF THE BILIARY TRACT, WITH SPECIAL REFERENCE TO LATENT (OR MASKED) AND TYPHOID INFECTIONS.[1]

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THAT infections of the biliary tract are by no means uncommon has long been recognized. The gross and quite obvious manifestations of such infections—suppurative cholangitis, suppurative, phlegmonous, and gangrenous cholecystitis, certain forms of abscess of the liver, etc.— were well recognized and quite accurately described by our forefathers. That these disorders, however, by no means comprise the totality of biliary infections has been demonstrated only during recent years, and even now the full import of other less obvious infections is not as widely known nor as keenly appreciated as is desirable. There are much more subtle infections of the biliary tract—ill-understood, frequently overlooked, and commonly misinterpreted: infections that often give rise to no symptoms, at least no noteworthy symptoms, for many years, if at all; infections diverse in their pathological lesions, variable in their sequels, and often complex and aberrant in their clinical manifestations; indeed, of many the symptomatology has not yet been completely worked out.

The observations to which I invite your attention are based primarily upon a statistical study of the clinical and other phenomena of 216 patients operated upon by Dr. John B. Deaver at the German Hospital, Philadelphia, during the last six years (1900 to 1905 inclusive).[2] My personal work has comprised a study of the gall-bladders removed by Dr. Deaver; of the pathological lesions at the necropsy in some of the fatal cases and in other cases (from the medical as well as the surgical wards) in which operation was not done; of the pathological lesions at the operation on some of the patients;[3] and a bacteriological study begun at the time of operation in seventy of the cases, and at the necropsy in a few of the fatal cases. I had thought to add certain details of my clinical experience gained elsewhere, but I have finally determined,

[1] Part I of the Mütter Lecture of the College of Physicians of Philadelphia, delivered December 1, 1905.

[2] It is with much pleasure that I here record my indebtedness to Dr. Deaver for his many courtesies in connection with the study. Not only has he afforded me opportunities to witness many of his operations, but he has also generously permitted me to make a statistical study of his case-histories. I am also indebted to Dr. James R. Freeland, one of the resident physicians at the German Hospital, for assistance in compiling the statistics.

[3] The living as contrasted with the dead pathology, as Dr. Deaver delights to call it.

in this communication, to deal only with the German Hospital material.

The somewhat restricted aspects of the broader subject of infections of the biliary tract that I have elected to discuss with you may be divided more or less artificially into two parts: the one comprising the more immediate, the second the more remote consequences of biliary infection. In many cases, however, the one fades almost imperceptibly into the other, and no sharp line of demarcation can be drawn between them. In this, Part I, I shall ask your attention especially to the pathways of infections of the biliary tract and to latent (or masked) and typhoid infections; in Part II, I shall discuss certain remote consequences of biliary infection, notably cholelithiasis, calculous cholecystitis, and adhesions of the upper abdomen, and I shall also direct your attention to the general principles of treatment and the indications for surgical intervention.

THE INFECTIOUS AGENTS.

The bacteriology of infections of the biliary tract has been studied by a large number of investigators—postmortem, at operation, and experimentally. Although considerable interest attaches to postmortem studies, the results are frequently vitiated by more or less obvious factors, and they cannot be relied upon implicitly unless the examinations are undertaken within a very short time after death. The conditions at operation, however, are quite different and the results much more trustworthy—although in subsiding or long-standing infections the primary infective agent may not be recovered, since it may have died out or have become overgrown by secondary invaders.

Although I have made some study of the bacteriology of the biliary tract at necropsies, these have been comparatively few and non-systematic, and they were undertaken largely because of special interest in individual, particularly typhoid fever, patients. At the German Hospital, however, we have studied the bacteriology of the biliary tract of seventy of the patients[1] operated upon by Dr. Deaver. The results are as follows:

	Cases.	Per cent.
Bacillus coli communis was found in	23	32.8
Bacillus typhosus was found in	7	10.0
Staphylococcus pyogenes aureus was found in	2	2.9
Streptococcus pyogenes was found in	1	1.4
Staphylococcus pyogenes albus was found in	1	1.4
Bacillus coli and Staphylococcus aureus were found in	2	2.9
No bacteria were found in	34	48.6

[1] Fifty of these cases have already been reported by Dr. G. P. Müller, assistant pathologist to the German Hospital: The Pathology of Cholecystitis, Brooklyn Med. Journ., 1905, xix, 11

In general these results do not differ materially from those obtained by other observers, although the variety of bacteria is not as great as that of all other observers combined. Other bacteria isolated from the biliary tract comprise the cholera bacillus, Bacillus subtilis, Bacillus capsulatus aërogenes, leptothrix, etc. Biliary infections complicating pneumonia and influenza suggest the possibility of the pneumococcus and the influenza bacillus respectively being the etiological agent (general blood infection or a local infection from the duodenum), but as far as I know these organisms have not yet been isolated from the local lesions. In addition to the aforementioned bacteria I am inclined to attach some etiological importance to anaërobic bacteria—which abound in the intestine. I have long believed that these organisms play a not inconspicuous part in the etiology of appendicitis, and I am quite prepared to believe the same of infections of the biliary tract. A most suggestive study of this entire question has recently been published by Lippmann.[1]

THE PATHWAYS OF INFECTION.

The pathways whereby the biliary tract may become infected are several: (1) The diverticulum of Vater and the common bile duct; (2) the portal circulation; (3) the systemic circulation; (4) the lymphatic circulation; and (5) directly through the wall of the gall-bladder or the gall ducts from the peritoneum.

1. *Infection from the duodenum by way of the diverticulum of Vater and the common bile duct* has long been looked upon as at once the most likely and the most common source of biliary infections, but whether with good reason remains to be decided. Its possibility cannot be denied, its probability may be conceded, but the exact factors concerned in its mechanism have not yet been determined definitely. In this connection we have to bear in mind that although the frequency of Bacillus coli communis and of Bacillus typhosus in infections of the biliary tract suggests an intestinal source, these bacteria find a direct pathway from the intestine to the liver by way of the portal circulation. Furthermore, as a number of observers have pointed out, whereas the jejunum and the ileum always contain many bacteria, the duodenum when free from food is often bacteria-free; certainly, in health its bacterial-content is small and it does not contain the bacteria often found in cholangitis, cholecystitis, etc. It is quite conceivable, however, indeed it is quite likely, that in conditions of disease of the upper intestine when bacteria are present in the duodenum the biliary tract may become infected by way of the diverticulum of Vater;

[1] Le microbisme biliaire normal et pathologique, Paris, 1904

doubtless many of the cases of so-called catarrhal jaundice following gastroduodenitis arise in this fashion. But there are at least two important factors opposing a ready ascending infection of the biliary tract: The one, the action of the sphincter of the diverticulum, which has been estimated by Oggi[1] as exerting a force equal to a pressure within the common bile duct of 700 millimeters of water; the second, the influence of the free flow of bile. Indeed, it is doubtful whether infection of the biliary tract ever takes place by way of the diverticulum of Vater in the absence of stasis of the bile.

One of the most important, if not the most important, factor in preventing such infection is the free flow, that is the regular periodic expulsion, of the bile—the free flow of the bile rather than the bile itself, since we now know, contrary to former opinions, that the bile is a quite favorable medium for the growth of bacteria.

Assuming infection by way of the diverticulum of Vater, we must credit the invading bacteria with some degree of intelligence—else why in their onward march do they deviate to the left rather than to the right when they encounter the fork in the diverticulum? As far as we know the pancreatic duct is by no means as frequently infected as the biliary passages. The influence of differences in pressure in the two ducts cannot be of commanding importance, since in this event the secretion of the one would frequently be forced into the other. Should this be the common source of biliary infection we must also assume that in conditions of ordinary infection the pancreas and the liver are quite capable of dealing with the invading bacteria, and that it is only because the gall-bladder has no analogue in the pancreatic duct that the biliary tract is so much more commonly the seat of infection. In this connection we may contrast the infrequency of intrahepatic lithiasis with the infrequency of pancreatic lithiasis: possibly many of the causative factors of both are quite alike. We must also explain why bacteria, innocuous or comparatively innocuous in the intestine, become mischievous immediately they pass the portal of the diverticulum. Possibly the conditions are analogous to those encountered in the vermiform appendix where defective drainage plays such an important etiological role. Finally, it is important to emphasize the fact that were typhoid cholecystitis, for instance, an ascending infection micro-organisms other than the typhoid bacillus, such as Bacillus coli communis, streptococci, staphylococci, etc., would probably frequently be found in association with the typhoid bacillus, and that the regularity with which the typhoid bacillus is recovered in pure culture from the gall-bladder in typhoid fever renders it unlikely that the infection is an ascending one.

[1] Quoted by Naunyn, Zur Naturgeschichte der Gallensteine und zur Cholelithiasis, Grenzgeb. der Med. und Chir., 1905, xiv, 537.

In favor of the view that infection may occur by way of the diverticulum of Vater, I may mention that bacteria have been found in the diverticulum under apparently normal conditions; that Lippmann[1] recently has isolated bacteria from the middle and even the upper third of the apparently normal common duct—in numbers decreasing upward; that in the presence of gallstones, bacteria are not infrequently more numerous in the lower end of the common bile duct than elsewhere in the biliary tract; that as we might expect *a priori* motile bacteria, such as Bacillus coli communis, Bacillus typhosus, etc., are much more commonly the invaders than non-motile organisms, such as streptococci, staphylococci, pneumococci, etc.; that experimentally infection has been found to occur with readiness when the flow of the bile has been impeded —in which relation the early experimental work of Gilbert and Girode[2] and others merits attention; and that, finally, I believe significant deductions may be drawn from the recently published and very interesting experiments of Bond[3] on ascending currents in mucous glands and gland ducts. Bond seems to have proved that by some means or other, and under certain conditions, particles of an insoluble substance, such as indigo, inserted into the orifice of a mucous canal or duct are conveyed along the mucous channel in a direction reverse to that taken by the contents of the tube, or by the secretion or excretion of the glands along such ducts —that is, for example, from the duodenum to the gall-bladder, from the urethra to the urinary bladder, etc. Bond believes that this phenomenon is not due to physical agency alone, such as capillary attraction, since it is absent in the non-living tube; and that the transference of the particles in empty tubes and ducts is one, and that there are several other reasons for regarding the mucus that coats the walls of the tube or duct as the vehicle in which the particles are carried. The essential factors seem to be a living tube the walls of which are partially, if not wholly, in apposition and lined with a mucous secretion. Further observation is said to be necessary to ascertain whether a reverse current—a sort of backwater—is present in all mucous channels, or whether it only exists where the normal outgoing current of secretion or excretion is interfered with. Such a back current is probably present to a certain extent normally, although it is much increased by any agency, such as a fistula, which starts a flow of mucus from the other end of the canal.

The application of the foregoing observations to the possibility and the phenomena of ascending infections of the biliary tracts must be quite obvious. Thus, while we cannot deny that infection of

[1] Loc. cit.

[2] Contribution a l'étude bacteriologique des voies biliaires, Comp. rend. Soc. Biol., 1890, ii, 739.

[3] Ascending Currents in Mucous Glands and Gland Ducts, Brit. Med. Jour., 1905, ii, 232.

the biliary passages may and probably does occur in some cases by way of the diverticulum of Vater, we are forced to the conclusion (1) that certain ill-understood factors exercise in the process a more or less unknown part, and (2) that in the past we have unquestionably overestimated the importance and the significance of this source of infection.

2. *Infection by way of the portal circulation* is doubtless a common source of biliary infection, although it was for a long time overlooked. Definite experimental proof that the bile may become infected from the circulation was furnished years ago by Blachstein[1] and Welch,[2] and their results have since been amply confirmed and amplified by a number of investigators, notably Sherrington,[3] Desoubry and Porcher,[4] Nocard,[5] Fütterer,[6] Adami,[7] Ford,[8] Wrzosek,[9] Lartigau,[10] Doerr,[11] and others. Though there have been a few dissenters, such as Carmichael,[12] the recent very accurate studies leave no room for doubt that bacteria transported to the liver by the portal circulation may be found in the bile. Although one may well concede, indeed maintain, that under normal circumstances bacteria carried to the liver by the portal circulation are there destroyed by the bactericidal properties of the liver cells, he must admit a limit to such bactericidal properties and that when overcome bacteria may pass over into the biliary passages. Among others, Lartigau's work is especially conclusive. Having tied the common bile duct in a number of animals he fed the animals Bacillus pyocyaneus, and was subsequently able to recover this organism, sometimes alone, sometimes associated with Bacillus coli communis, from the gall-bladder of almost one-half the animals. Adami having shown that, under apparently normal conditions, bacteria may be found in the deeper layers of the intestine, in the portal circulation, and in the liver, suggests that they invade the

[1] Intravenous Inoculation of Rabbits with the Bacillus coli communis and the Bacillus typhi abdominalis, Johns Hopkins Hosp. Bull., 1891, ii, 96.

[2] Additional Note Concerning the Intravenous Inoculation of the Bacillus typhi abdominalis, Johns Hopkins Hosp. Bull., 1891, ii, 121.

[3] Experiments on the Escape of Bacteria with the Secretions, Jour. Path. and Bact., 1892–93, i, 258.

[4] De la presence de microbes dans le chyle normal chez le chein, Compt. rend. Soc. Biol., 1895, ii, 101.

[5] Influence des repas sur la penetration des microbes dans le sang, Sem. méd., 1895, xv, 63.

[6] Wie bald gelangen Bacterien welche in die Portalvene eingedrungen sind in den grossen Kreislauf und wann beginnt ihre Ausscheidung durch die Leber und die Niere, Berl. klin. Woch., 1899, xxxvi, 58.

[7] On Latent Infection and Subinfection, Jour. Amer. Med. Assoc., 1899, xxxiii, 1509, 1572.

[8] Bacteriology of Healthy Organs, Trans. Assoc. Amer. Phys., 1900, xv, 389.

[9] Experimentelle Beiträge zur Lehre von dem latenten Mikrobismus, Virchow's Archiv, 1904, clxxviii, 82.

[10] The Relation of Bacteria to the Development of Gallstones, California State Jour. of Med., 1906, iv, 17.

[11] Experimentelle Untersuchungen über das Fortwuchern von Typhusbacillen in der Gallenblase, Centralbl. für Bakt., 1905, xxxix, 624; Wien. klin. Woch., 1905, xviii, 884.

[12] The Effect of Injection of Micro-organisms into the Portal System on the Sterility of the Bile in the Gall-bladder, Jour. Path. and Bact., 1902–03, viii, 276.

portal circulation through the aid of the leukocytes—which are especially active during digestion, carrying foodstuffs, foreign matters, bacteria, etc., between the epithelial cells to the lymphatic radicles and the portal venules. Ordinarily most of the bacteria are destroyed, probably in large part through the bactericidal property of the normal living intestinal mucosa, as maintained by Rolly and Liebermeister,[1] in part also by the leukocytes, the lymph nodes, and the endothelium of the liver; sometimes, however, they pass through the liver and gain the bile; in other cases, by way of the thoracic duct, as maintained by Wrzosek and others, they invade the general circulation, and, as well pointed out by Ford, may be found in the liver, kidneys, etc., of apparently normal animals. This is the latent infection of Adami and certain French and German writers. Recently, Nicholls[2] has described what he designates a simple method of demonstrating the presence of bacteria in the mesentery of normal animals—a method based upon histological procedures, and which, although suggestive, lacks the trustworthiness accorded to cultural methods.

3. *Infection by way of the systemic circulation,* although possibly not an exceedingly common source of infection of the biliary tract, should not be entirely ignored. Its importance as a possible source of infection has been enhanced since we have ascertained the frequency, in fact almost the regularity, of bacteremia in the great majority of infectious processes—typhoid fever, pneumococcic and pyococcic infections, etc.; and experimental proof that the biliary passages may become thus infected was furnished, as already mentioned, years ago by Welch and Blachstein, and quite recently by Doerr. Doerr found that micro-organisms injected into the general circulation of rabbits appear in the gall-bladder within a few hours, and that typhoid bacilli and colon bacilli multiply in the gall-bladder and may be recovered therefrom in pure culture even after the lapse of four months. The resulting lesions were usually catarrhal, but they might become purulent. On the contrary, organisms introduced subcutaneously or intraperitoneally did not lead to infection of the gall-bladder. The occurrence of cholecystitis and cholangitis as a complication of general infections, such as influenza, pneumonia (recently reported upon by Richardson,[3] Anders,[4] etc., and studied experimentally by Brion and Kayser),[5] etc., also suggests the likelihood of the infection occurring by way of the general circulation; but one must concede the possibility

[1] Experimentelle Untersuchungen über die Ursachen der Abtötung von Bakterien im Dünndarm, Deut. Arch. f. klin. Med., 1905, lxxxiii, 413.

[2] A Simple Method of Demonstrating the Presence of Bacteria in the Mesentery of Normal Animals, Jour. Med. Research, 1904, xi, 455.

[3] Acute Inflammation of the Gall-bladder, AMER. JOUR. MED. SCI., 1898, cxv, 629.

[4] Cholecystitis as a Complication of Croupous Pneumonia, Amer. Med., 1904, ix, 431.

[5] Kunstliche Infektion der Gallenblase mit Pneumokokken nach Choledochusresektion, Grenzgeb. der Med. und Chir., 1903, xii, 677.

of the local biliary infection being due to organisms other than those occasioning the primary infection, and that the complicating infection may occur by way of the portal circulation or the diverticulum of Vater. Infection by way of the hepatic artery is a descending infection and operates as does infection carried by the portal circulation—since both circulations commingle at the periphery of the liver lobules; but infected blood carried by the cystic artery may, although probably rarely, lead directly to infection of the gall-bladder without the intermediation of infected bile.

4. *Infection by way of the lymphatic circulation* has been suggested by G. P. Müller,[1] who, pointing out its likely mechanism, reports a case that he believes illustrates this manner of infection. I am inclined to agree with him, although this is probably a most infrequent source of infection.

5. *Direct infection through the wall of the gall-bladder* or of the ducts from the peritoneum has been suggested as a possibility; but excluding cases of general peritonitis in which the gall-bladder may participate secondarily in the more widespread lesions and in which the mechanism of the local infection may be quite obvious, it is doubtful if infection of the biliary tract directly from the peritoneum can occur in the absence of adhesions—in which event it is probably an infection by way of the lymphatic circulation. In this connection, however, we must also bear in mind that the adhesions themselves are an evidence of past infection, and that an obvious infection in the presence of old adhesions is much more likely the relighting of an old, latent infection, rather than a new infection transmitted directly through the walls of the gall-bladder or the gall ducts.

The pathways of biliary infection doubtless vary with the infecting agent. Bacillus coli infections, which must be looked upon as the most common, doubtless occur most frequently by way of the portal circulation. In most cases the liver in full functional activity is enabled to destroy or render innocuous such colon bacilli as may pass the barrier of the intestinal mucosa and be transported to it; but should the physiological activity of the liver become impaired, or should the colon bacilli become of heightened virulence, as happens in inflammatory and ulcerative processes of the intestine, bacilli of attenuated virulence may pass over into the biliary circulation and, being excreted with the bile, set up a low grade biliary catarrh. This commonly passes unnoticed by the patient, but it is one of the most important factors in the etiology of gallstones, as it is also the most important factor in the complications of gallstones. We must admit, however, that in the event of gastroduodenitis colon bacilli may infect the biliary passages by way of the diverticulum of Vater and the common duct; in this event, the lesions are likely to be more abrupt in onset and more manifest clinically.

[1] The Pathology of Cholecystitis, Brooklyn Med. Jour., 1905, xix, 11.

Typhoid infection may occur by way of the portal circulation, by way of the systemic circulation, and by way of the diverticulum of Vater. I am inclined to believe that the frequency of gall-bladder infection in typhoid fever finds one of its explanations in the three sources whereby the biliary tract may become infected—although the systemic and the portal circulations are the more important.

Pneumococcic, pyocoecic, influenzal infections, etc., are doubtless in many cases general systemic infections; in some cases the infection is probably by way of the diverticulum of Vater—but the subject still requires considerable elucidation.

The Results of Biliary Infection. The results of biliary infection vary with the virulence of the infecting micro-organism and the resistance offered by the subject; they may be insidious or frank in onset, acute, subacute, or chronic in course, and slight or extremely severe in character. The frank acute cholangitis and cholecystitis are usually so obtrusive in their manifestations as scarcely to escape observation; and although they sometimes present diagnostic difficulties these are usually overcome with care and the disease is correctly recognized. When, however, the infection is more insidious in onset and subacute or chronic in course and the infecting micro-organisms of low virulence, the resulting lesions are of such nature and the symptoms so slight or altogether absent that they are often ill-understood, misinterpreted, and referred to organs other than their real source.

Since it is manifestly impossible, even if it were desirable (which on this occasion it is not), to review in detail the manifold phenomena of infections of the biliary tract, I have elected to ask your attention to several of the most interesting aspects of the subject only; that is, latent or masked infections, of which many of the typhoid (and paratyphoid) infections serve as a type.

LATENT OR MASKED INFECTIONS.

The introduction of micro-organisms of low virulence into the biliary tract may be unattended by pathological lesions, and this is the more likely to be the case if the ducts are patent and the flow of bile unobstructed. Comparatively virulent micro-organisms also may sometimes be disposed of, if the biliary drainage is free and unimpeded, but usually serious and even fatal forms of disease are thus provoked—suppurative cholangitis and suppurative and gangrenous cholecystitis. Between the extremes of innocuousness or comparative innocuousness and quick and early disaster lie the great majority of cases of biliary infection.

As in other mucous canals, the immediate result of infection of the biliary tract is the production of a catarrh, with the usual inflammatory phenomena—œdema and congestion of the mucous mem-

brane, increased production of mucus, and desquamation of epithelium. If the biliary circulation is free and unimpeded the results of this catarrh are washed away for the most part, but on account of special local conditions (largely dynamic) they are likely to accumulate, to become accentuated, and to persist in the gall-bladder. In the event of obstruction to the free flow of bile these are all the more certain to occur. In many cases the lesions thus provoked are entirely latent or unannounced by noteworthy or unequivocal symptoms; they may pursue a short course, or they may continue for years; and they are one of the most important factors, in fact, the important factor, in the etiology of gallstones. These latent or masked infections are doubtless due to different micro-organisms in different cases, but since a large majority of them are due to the typhoid bacillus (and its brother the paratyphoid bacillus) they may be studied from the point of view of typhoid infections.

TYPHOID INFECTIONS.

Although biliary complications of typhoid fever were by no means unknown to our forefathers, having been noted even by Louis in 1838 and by Murchison in 1862, the noteworthy additions to our knowledge of the subject are of quite recent date. The early history of the development of our knowledge was well reviewed in 1897, by Mason,[1] who collected 14 cases; in 1897, by Osler;[2] in 1898, by Da Costa,[3] who collected 58 cases; and in 1899, by Camac,[4] who collected 115 cases. Since then the subject has been studied by a large number of investigators, and we now have comparative unanimity regarding the following points: (1) That the typhoid bacillus is regularly present in the gall-bladder, and commonly in pure culture, in practically all cases of typhoid fever—indeed, it is the one region of the body from which a pure culture of the organism is most likely to be obtained; (2) that the typhoid bacillus may persist in the gall-bladder, as well as within gallstones, weeks, months, even years, after the patient has recovered from an attack of typhoid fever; (3) that cholangitis and cholecystitis (catarrhal, suppurative, and gangrenous) are by no means infrequent complications of typhoid fever; and (4) that a history of antecedent typhoid fever may be obtained in many cholelithitic and cholecystitic subjects. Furthermore, it is important to bear in mind, as has recently been

[1] Gall-bladder Infection in Typhoid Fever, Trans. Assoc. Amer. Phys., 1897, xii, 23.

[2] Hepatic Complications of Typhoid Fever, Trans. Assoc. Amer. Phys., 1897, xii, 378.

[3] Significance of Jaundice in Typhoid Fever, Amer. Jour. Med. Sci., 1898, cxvi, 1; Cases of Typhoid Cholecystitis Ending in Recovery, ibid., 1899, cxviii, 138.

[4] Cholecystitis Complicating Typhoid Fever, Amer. Jour. Med. Sci., 1899, cxvii, 275; Gall-bladder Complications of Typhoid Fever, Johns Hopkins Hosp. Reports, 1899–1900, viii, 339.

insisted upon by Doerr,[1] Forster and Kayser,[2] Brion and Kayser,[3] and as is suggested also by my own studies, that many of these subjects—some apparently healthy and others ill only with a local disorder—are unconscious harborers and disseminators of the typhoid bacillus. The continuous reinfection of the intestinal tract by the frequent discharge of virulent typhoid bacilli from a chronically infected gall-bladder may be of much significance to the individual, but it is of even more significance from an epidemiological point of view—since there can be little doubt that these apparently healthy harborers of typhoid bacilli spread the infection and sometimes may even give rise to more or less extensive epidemics.

If, in some cases, the typhoid bacillus is present in the gall-bladder without exciting pathological lesions, in many cases lesions are produced; all degrees are encountered—from the mild catarrh to the severest suppurative and gangrenous processes with perforation of the gall-bladder. What I desire to emphasize, however, is the fact that in many cases the biliary infection though present is altogether latent clinically, and that although in other cases it occasions demonstrable symptoms, the true nature of these is often masked and they escape correct interpretation. First, there are cases in which during the course of typhoid fever a noteworthy enlargement of the gall-bladder occurs; but the biliary ducts being patent, and the drainage therefore sufficient, and the patient's sensibilities somewhat obtunded, there is no complaint and the disorder escapes clinical recognition—unless perchance systematic and repeated examinations of the gall-bladder region are undertaken; in this event a more or less enlarged and tender gall-bladder may be encountered. I believe that it is really surprising how frequently this occurs; shall I also say surprising how frequently it goes undetected? Second, there are cases in which a little epigastric discomfort, perhaps slight nausea, in some cases actual pain, is complained of, and examination reveals an enlarged and tender gall-bladder. I have come to regard nausea during the course of typhoid fever, when not due to other obvious cause, as quite significant of gall-bladder infection, although, of course, it may be due to other factors. Third, there are cases in which announced by the ordinary symptoms an acute cholecystitis or cholangitis develops —often severe in type. This is probably more common during or after convalescence than during the course of the infection. Such is often the severity of the symptoms in these cases that I invite a surgeon to see the patient with me: his advice is always valuable, and although the infection commonly subsides spontaneously, an operation may be called for at any time—in which event it is

[1] Loc. cit.

[2] Ueber das Vorkommen von Typhusbazillen in der Galle von Typhuskranken und "Typhus bazillenträgern," Münch. med. Woch., 1905, lii, 1473.

[3] Neuere Klinisch-bacteriologische Erfahrungen bei Typhus und Paratyphus, Deut. Archiv. f. klin. Med., 1906, lxxxv, 525.

desirable that the surgeon should have had an opportunity to watch the progress of the disorder.

There are, in addition, several other aspects of typhoid infection of the biliary tract worthy of study:

Relapse in Typhoid Fever. First of all, I must point out the significant fact, first insisted upon I believe by Musser, that in reality many of the so-called relapses in typhoid fever are by no means relapses in a restricted sense, but rather manifestations of some local infection of the body—often of the biliary tract, cholecystitis. The more attentively I study my typhoid fever patients the less inclined I am to pass by a so-called relapse as a relapse only; in fact, I feel somewhat chagrined if I am unable to put my finger upon some definite cause for the return of the fever. In many cases a gall-bladder infection will be found; in other cases, an infection of the urinary tract; in others, fecal impaction, furunculosis, osteitis, periostitis, etc., while in still other cases the increased flow of infected bile occasioned by a return to a liberal diet, or other factors, may determine what may be looked upon as a real relapse—commonly reinfection from an infected gall-bladder. But in most cases, persistent search for a definite local infection will be rewarded with success. These, especially the gall-bladder infections, have important surgical bearings, and should be attentively studied. It is true that the inflammatory phenomena frequently subside spontaneously and the indication for the surgical intervention passes away; but these infections are a fruitful source of mischief in later life—often causing gallstones, subacute and chronic cholecystitis, pericholecystic adhesions, and divers other ills that commonly are grouped with the congeries of symptoms designated "stomach trouble."

Primary Typhoid Cholecystitis. Then I must ask your attention to the occurrence of a primary typhoid cholecystitis and cholangitis—an infection of the biliary tract without other evidence of past or present typhoid infection. My attention was directed to this subject in 1901, by Pratt,[1] who, reporting two cases, referred to three other cases in the literature (Cushing, Mitchell, and Hunner). Since then the subject has been studied by Stockton and Lytle,[2] Burlew,[3] Stewart,[4] Rudolph Müller,[5] Doerr,[6] Forster and Kayser,[7] Blumenthal,[8] Findlay and Buchanan,[9] etc.

[1] Typhoid Cholecystitis, Amer. Jour. Med. Sci., 1901, cxxii, 584.

[2] New York State Med. Jour., 1902, ii, 232.

[3] Typhoid Cholecystitis and Calculi without any Evidence of Typhoid Fever, Medicine, 1903, ix, 731.

[4] Primary Typhoid Cholecystitis, Amer. Med. 1904, vii, 1018.

[5] Cholecystitis und Cholangitis als Ursache von positiver Gruber-Widalscher Reaktion bei Ikterus, Zeit. f. Heilk., path. Anat. Heft, 1905, xxvi, 263.

[6] Loc. cit.

[7] Loc. cit.

[8] Ueber das Vorkommen von Typhus- und Paratyphusbazillen bei Erkrankungen der Gallenwege, Münch. med. Woch., 1904, xxxvii.

[9] A Case of Typhoidal Cholecystitis, Glasgow Med. Jour., 1906, lxv, 177.

The typhoid bacillus[1] was isolated from the gall-bladder of 7 of Dr. Deaver's 216 patients; and from the gall-bladder of another patient operated upon in 1906.[2] All of these 8 patients were women. In 4 no history of previous typhoid fever, nor of concurrent typhoid fever (in the commonly accepted sense), could be obtained.

The first patient, K. H., aged forty-nine years, was admitted to the hospital June 22, 1903. The first attack of pain occurred ten years prior to admission, and the pain recurred about twice a year thereafter. Operation revealed the gall-bladder thickened and contracted, extensive adhesions between the gall-bladder, the duodenum, and the stomach, a cholecystogastric fistula, and many gallstones in the adhesions. Cholecystectomy was done, and the patient recovered.

The second patient, K. C., aged fifty-six years, was admitted to the hospital August 24, 1903. The first attack of pain occurred four years prior to admission; recurrences were frequent. Operation revealed the gall-bladder enlarged, necrotic, and ulcerated, about fifty gallstones and 150 c.c. of pale, yellowish pus in the gall-bladder, and many adhesions between the gali-bladder, the duodenum, and the stomach. Cholecystectomy was done, and the patient recovered.

The third patient, E. H., aged twenty-seven years, was admitted to the hospital March 11, 1904. The first attack of pain occurred three weeks prior to admission. Operation revealed suppurative cholecystitis, about 100 c.c. of yellowish purulent material in the gall-bladder, one gallstone obstructing the cystic duct, and adhesions between the gall-bladder, the liver, the duodenum, and the omentum. Cholecystectomy was done, and the patient recovered.

The fourth patient, A. C., aged forty-seven years, was admitted to the hospital April 27, 1904. The first attack of pain occurred two years prior to admission; recurrences were frequent. Operation revealed suppurative cholecystitis, many stones, and about 100 c.c. of bloody, yellowish, purulent fluid in the gall-bladder, and a few pericystic adhesions. Cholecystectomy was done and the patient recovered.

The fifth patient, S. W., aged fifty-six years, was admitted to the hospital June 22, 1903. Nine weeks prior to admission the patient was taken ill with what was said to have been typhoid fever—chills, fever, anorexia, headache, vomiting, etc. Four weeks later pain

[1] The following biological characteristics of an organism under investigation were looked upon as proof of its being the typhoid bacillus: An actively motile bacillus that grew well on all the ordinary laboratory media; a delicate, translucent, slightly bluish, or iridescent growth with irregular or serrated edges on agar surfaces; a whitish, almost if not quite invisible, growth on potato; no gas production in glucose, saccharose, or levulose media; no indol production; no coagulation and no (or very slight) acidulation of milk; and a positive Gruber-Widal reaction with known typhoid serum in dilutions of 1 to 50 or 1 to 100 or higher.

[2] This patient, of course, had not been observed at the time the Lecture was delivered, but the notes of the case are included here for obvious reasons.

in the gall-bladder region was complained of and a mass was detected. Operation revealed the gall-bladder enlarged, necrotic, ulcerated, and perforated; it contained one stone and a considerable amount of dark, purulent bile. There were many adhesions between the gall-bladder, the pylorus, the duodenum, the colon, and the omentum. Cholecystostomy with drainage was done, and the patient recovered.

The sixth patient, M. R., aged forty-two years, was admitted to the hospital January 30, 1905. She had had typhoid fever fifteen years previously. The first attack of pain occurred one month after the typhoid fever; recurrences were frequent. Operation revealed a chronic cholecystitis, twenty gallstones in the gall-bladder, one stone in the common duct, and many adhesions between the gall-bladder, the liver, the duodenum, the stomach, and the omentum. Cholecystostomy with drainage was done, and the patient recovered.

The seventh patient, J. Y., aged thirty-eight years, was ill in the German Hospital with typhoid fever from April 25 to May 30, 1905. On June 7th she had what was called indigestion. On June 22d the first definite colic occurred. On July 2d she was readmitted to the hospital. Operation revealed an enlarged gall-bladder with unusually thickened walls (up to 14 mm.), one stone and about 60 c.c. of pus in the gall-bladder, and many adhesions between the gall-bladder, the edge of the liver, and the omentum. Cholecystostomy with drainage was done and the patient recovered.

The eighth patient, P. E., aged forty years, was admitted to the Hospital July 2, 1906. She had had typhoid fever fourteen years previously, and subsequently has suffered repeatedly from "stomach trouble." The first definite gallstone colic occurred eleven days prior to admission to the hospital; there were two subsequent colics. Operation revealed the gall-bladder enlarged, thickened, and congested; its mucous membrane was completely necrotic, detached, forming a veritable cast; and there were fifty to seventy gallstones in the gall-bladder. Cholecystectomy was done and the patient recovered. On August 4, 1906 (after convalescence), the patient's blood yielded a positive Gruber-Widal reaction with the typhoid bacillus.

In addition to these eight patients from whose gall-bladders the typhoid bacillus was isolated, two other rather interesting patients were observed:

The ninth patient, C. S., a male, aged thirty-five years, was admitted to the hospital March 2, 1905. He had had his first attack of colic four years before admission; a second attack three years before admission; typhoid fever fifteen months before admission; and a third attack of colic three weeks before admission. Operation revealed an enlarged and distended gall-bladder, about 200 c.c. of clear, brownish-green bile in the gall-bladder, three gallstones in the common duct, and no adhesions. Cholecystos-

tomy with drainage was done. The patient had been jaundiced for a long time, and died of capillary oozing and cholemia. His blood serum gave a positive Gruber-Widal reaction with the typhoid bacillus, but the colon bacillus only was isolated from his gall-bladder (at the time of operation).

The tenth patient, M. O., a female, aged fifty-five years, was admitted to the hospital August 11, 1905. She had had typhoid fever seven years prior to admission. The first attack of colic occurred four years prior to admission. Operation revealed a thickened and atrophic gall-bladder, one stone in the gall-bladder, adhesions between the gall-bladder, the liver, the duodenum, and the stomach. Cholecystostomy with drainage was done, and the patient recovered. Her blood serum gave a positive Gruber-Widal reaction with the typhoid bacillus. No cultures were taken.

This primary typhoid cholecystitis is of much importance from several points of view, and heretofore has been insufficiently studied. The first four cases just cited are apparently examples of primary typhoid infection of the biliary tract; the fifth, sixth, seventh, eighth, and tenth cases are obviously examples of a local infection persisting after the general infection had subsided—acute in the fifth and seventh, chronic in the sixth, eighth, and tenth cases. In the sixth case it is not unlikely that the typhoid bacillus was harbored in the gall-bladder for fifteen years—since the first attack of colic occurred one month after an attack of typhoid fever, recurrences of the colic were frequent during the subsequent fifteen years, and the typhoid bacillus was recovered from the gall-bladder at operation. It is not improbable also that the typhoid bacillus was carried in the gall-bladder fourteen years in the eighth patient (the duration of the symptoms designated "stomach trouble"), ten years in the first patient, four years in the second, and two years in the fourth—the duration of the symptoms in the respective patients; but, of course, one cannot exclude the possibility of typhoid infection of an already infected gall-bladder. This is true also of the ninth patient, in whom it is furthermore interesting to speculate whether or not the attack of typhoid fever was precipitated by infection from a chronically infected gall-bladder. The isolation of the colon bacillus only from the gall-bladder in this patient suggests the probability of subsequent Bacillus coli infection of the gall-bladder.

These cases of apparently long-standing typhoid infection of the gall-bladder recall several similar observations recorded in the literature; for instance, the case reported by Ramond and Faitout,[1] in which the typhoid bacillus was recovered from the gall-bladder six years after an attack of typhoid fever; Miller's[2] case, after

[1] Angiocholecystite a bacille d'Eberth, Comp. rend. Soc. Biol., 1896, iii, 1130.

[2] The Presence of Bacillus Typhosus in the Gall-bladder Seven Years after Typhoid Fever, Johns Hopkins Hosp. Bull., 1898, ix, 95.

seven years; von Dungern's[1] case, after fourteen years; Droba's[2] case, after seventeen years; Hunner's[3] case, after eighteen years; and Camac's[4] case, after twenty years. These cases serve also to emphasize the epidemiological significance of these unconscious carriers of typhoid bacilli—to which I have already alluded. Doubtless bacteriological investigation of the stools of chronic cholecystitic subjects would perhaps frequently disclose the typhoid bacillus. An interesting feature of many of the typhoid infections of the biliary tract is the seriousness of the lesions—well exemplified in the cases herewith reported.

The Gruber-Widal Reaction in Cases of Jaundice. Since the earliest days of the clinical use of the Gruber-Widal reaction in the diagnosis of typhoid fever, cases of so-called catarrhal (as well as other forms of) jaundice have been observed in which the serum reaction was positive—whence at first it was not unnaturally thought that possibly jaundice vitiated the diagnostic trustworthiness of the serum reaction. However, since we have come to recognize the importance and the frequency of typhoid infection of the biliary tract, since we have learned of the occurrence of a primary typhoid cholecystitis and cholangitis, we have come also to think that these cases of jaundice are examples of typhoid infection, and that the Gruber-Widal reaction is of much importance in determining the nature of the jaundice (infection). This question has been studied attentively recently by Zupnik,[5] Eckardt,[6] Königstein,[7] Libman,[8] Zevi,[9] Rudolph Müller,[10] Ludke,[11] Steinberg,[12] Blumenthal,[13] Netter and Ribadeau-Dumas,[14] Brion and Kayser,[15] etc.

In a number of cases of jaundice that have yielded a positive Gruber-Widal reaction the typhoid bacillus has been isolated from

[1] Ueber Cholecystitis typhosa, Münch. med. Woch., 1897, xliv, 699.

[2] Der Zusammenhang zwischen Typhusinfektion und Cholelithiasis, Wien. med. Woch. 1899, xii, 1141.

[3] A Case of Acute Suppurative Cholecystitis with Isolation of the Bacillus Typhosus Eighteen Years after an Attack of Typhoid Fever, Johns Hopkins Hosp. Bull., 1899, x, 163.

[4] Gall-bladder Complications of Typhoid Fever, Johns Hopkins Hosp. Reports, 1899-1900, viii, 353.

[5] Erfahrungen über die Gruber-Widal'sche Reaktion und Autoagglutination bei Typhus abdominalis, Ztsch. f. Heil., path. Anat. Heft, 1901, xxii, 334.

[6] Widal'sche Serumreaktion bei Weil'scher Krankheit, Münch. med. Woch., 1902, xlix, 1129.

[7] Ueber die agglutinierende Eigenschaft der Galle und des Serums beim Ikterus, Wien. klin. Woch., 1903, xvi, 985.

[8] Notes on the Widal Reaction, Med. News, 1904, lxxxiv, 204.

[9] Ueber die Gruber-Widal'sche Reaktion bei Ikterus, Wien. klin. Woch., 1904, xvii, 861.

[10] Loc. cit.

[11] Agglutination bei Autoinfektionen mit besonderer Berücksichtigung des Ikterus, Deut. Archiv. f. klin. Med., 1904, lxxxi, 34.

[12] Ueber Agglutination von Typhusbazillen durch das Blutserum Ikterischer, Münch. med. Woch., 1904, li, 469.

[13] Ueber die Bedeutung der Gruber-Widal'schen Reaktion bei Erkrankungen der Leber und der Gallenwege, Medizinische Klinik, 1905, i, 1227 (other ref.).

[14] Details sur l'agglutination dans trente-sept cas de typhoides and paratyphoides. Compt. rend. Soc. Biol., 1905, xlix, 373. (Other articles in the same volume.)

[15] Loc. cit.

the biliary tract—at operation or after death; and since it has been determined experimentally that the bile as such has little if any tendency to cause agglutination of the typhoid bacillus, it is only reasonable to look upon a positive serum reaction in cases of jaundice as evidence of typhoid infection of the biliary tract. Heretofore, for obvious reasons, we have had to be content with a diagnosis of cholecystitis and cholangitis; a noteworthy advance in our diagnosis would be the recognition of the etiological agent. When cholecystitis or cholangitis complicates pneumonia, influenza, typhoid fever, dysentery, etc., the natural inference is that the primary infective agent is the cause of the complication—an inference usually but not always borne out by the fact. When, however, the cholecystitis of cholangitis occurs independently of any manifest general infection, when other evidence of general or local infection cannot be detected, the recognition of the nature of the local biliary infection is beset with difficulties.

There can be little doubt that we have much to learn of the nature of certain ill-understood forms of jaundice—so-called febrile jaundice, infectious jaundice, Weil's disease, etc. The resemblance that many of these cases bear to typhoid fever has been frequently commented upon, and it has in fact been suggested that Weil's disease is in reality a modified form of typhoid fever. Possibly in many cases it is only typhoid infection of the biliary tract. That this may well be so is suggested by the extreme variability of the known lesions of typhoid infection of the biliary tract—from the mildest local catarrhal lesions to widespread and fatal suppurative cholecystitis, cholangitis, and multiple abscesses of the liver. Furthermore, it is interesting to bear in mind that jaundice sometimes occurs at the onset of typhoid fever, as in some cases reported by Ogilvie[1] and others, and that epidemics of so-called catarrhal jaundice are occasionally observed. Dalgeish,[2] for instance, has reported such an epidemic that occurred in Bloemfontein, which he says resembled in many respects the prevailing typhoid fever and was thought to be due to the typhoid bacillus.

It would be wise, therefore, in all cases of jaundice to undertake bacteriological studies of the blood and the feces; whether or not these be feasible, the Gruber-Widal reaction with the typhoid, paratyphoid, and other bacilli should not be neglected. I should be inclined to consider a positive reaction in a dilution of 1 to 50 or 1 to 100, or higher, conclusive evidence of typhoid infection, having in mind, of course, the possibility of previous typhoid fever. In some reported cases positive reactions have been obtained at much higher dilutions—1 to 1800 (Rudolph Müller) and higher.

[1] Jaundice in Typhoid Fever, Brit. Med. Jour., 1901, i, 75.
[2] An Epidemic of Catarrhal Jaundice Probably due to the Enteric Fever Bacillus, Lancet 1901, ii, 523.

REVIEWS.

DIE KRANKHEITEN DES VERDAUUNGSKANALS. By PAUL COHNHEIM, M.D. Berlin: S. Karger, 1905.

AMONG the many excellent treatises that have appeared recently on diseases of the stomach and intestine the present work deserves a place in the library of every practising physician. It is a practial hand-book for the diagnosis and treatment of diseases of the alimentary tract, not a reference-book for those who wish to study the pathology and the latest methods of laboratory diagnosis. The author says in his preface: "I have endeavored to show that in the great majority of cases it is possible to make an exact diagnosis by the history and the physical findings, and by that means apply a rational method of treatment without recourse to the armamentarium of a laboratory and the use of the stomach tube, which is so repulsive to most patients." The promise held out in the preface is fully redeemed in the text. Minute instructions are given in the first chapter in regard to the questions to be asked in taking the history. Each question is taken up separately and discussed at great length, the significance of the various data obtained from the patient being discussed in connection with the individual diseases. Palpation carried out by certain rules is said to yield all the information about the abdominal contents necessary for practical work. In this we cannot entirely agree with the author. Obrastzow's method is recommended for locating the greater curvature of the stomach and determining the presence of dilatation or ptosis. It consists in giving the patient two glasses of water to drink and then performing so-called percutory palpation with the tips of the fingers, the gastric area being recognized by *feeling the water* in the stomach. Inflation is thought unnecessary in ordinary cases and should be used only to determine whether a tumor is connected with the anterior wall of the stomach or is situated behind the viscus. The method in experienced hands is no doubt adequate and has the great advantage of being so much less unpleasant to the patient than inflation with a tube or by the generation of carbon dioxide. While the palpation of the liver and gall-bladder (if the latter is enlarged), of the spleen under certain conditions, and of movable kidneys is commonly practised, one may be permitted to doubt whether such organs as the cecum and appendix are accessible to palpation, as stated by the author. He says that "in a comparatively large number of cases the normal appendix can be felt as a cord-like structure

about as long as the little finger and as thick as a pencil, which can be rolled under the finger." The chapter on the examination of the stomach contents is one of the shortest in the book and contains only what is absolutely necessary for office work. Relatively more attention is devoted to the microscopic examination of the stomach contents and of the feces than in other text-books on the subject.

The classification of diseases of the stomach has been reduced to the simplest possible terms—namely, organic, constitutional, and symptomatic. Pathology is altogether ignored, and the various conditions are discussed altogether from the clinical standpoint. Those who still believe in the medical treatment of ulcer will find that subject discussed in the most systematic manner. In regard to the surgical treatment the author says: "The only conditions that call for surgical treatment in ulcer of the stomach are perforation and chronic hemorrhages; on the other hand, the surgeon is very frequently called upon to treat complications of ulcer scars and their consequences." The early diagnosis of cancer before a tumor is palpable, receives the attention which such a practical subject deserves.

"We have seen that it is comparatively easy, even in the absence of a palable tumor, first to diagnosticate carcinoma of the stomach as such, and second, to determine the localization of the tumor as far as necessary for purposes of treatment; for the treatment depends altogether on the seat of the neoplasm, and a knowledge of its seat is necessary for the internist in order to determine the indications for a surgical intervention." He condemns inflation of the stomach with effervescent powder in the presence of suspected cancer of the stomach, but advises simple inflation in order to determine whether the tumor belongs to the anterior or the posterior wall of the stomach.

A similar plan is followed in that portion of the book which is devoted to diseases of the intestine. The classification again is into organic, functional, and symptomatic; parasites of the intestine and diseases of the rectum are treated in separate chapters.

The brief chapter on appendicitis is disappointing. It is devoted almost entirely to the discussion of the differential diagnosis between appendicitis and "typhlitis stercoralis," and between the three forms of appendicitis: simple or catarrhal, perforative, and gangrenous. Cohnheim evidently clings to the theory of a "stercoral typhlitis," and, true to the plan of his book, ignores the controversy on this subject which has been carried on during the past years. Possibly he thinks the question has no practical importance, as he views the differential diagnosis purely from the standpoint of treatment: stercoral typhlitis or simple inflammation of the cecum, due to fecal accumulations, and simple or catarrhal appendicitis recover under conservative medical treat-

ment; while perforative, gangrenous, and the larval, as well as the recurrent form, require operation; but he has, to say the least, given too much prominence to this disputed clinical entity, stercoral typhlitis, to the neglect of other important conditions, the differential diagnosis of which is dismissed with a mere enumeration.

The text is agreeably diversified with short clinical reports of apposite cases, and an appendix contains a table for use in diagnosing diseases of the stomach without the use of a test breakfast; a collection of diet lists; a short abstract of balneotherapy and hydrotherapy, and a "clinical A B C of the most important digestive disturbances."

The book should prove useful as a guide to teachers and students and as a hand-book to practitioners, particularly on questions of treatment. R. M. G.

PATHOGENIC MICRO-ORGANISMS, INCLUDING BACTERIA AND PROTOZOA. A Practical Manual for Students, Physicians, and Health Officers. By WILLIAM HALLOCK PARK, M.D., Professor of Bacteriology and Hygiene, University and Bellevue Hospital Medical College, and Director of the Research Laboratory of the Department of Health, City of New York. Assisted by ANNA W. WILLIAMS, M.D., Assistant Director of the Research Laboratory. Second edition, enlarged and thoroughly revised. New York and Philadelphia: Lea Brothers and Co., 1905.

IN this book is found a very excellent exposition of the present-day conceptions of the relation of pathogenic bacteria and protozoa to disease. The subject is treated with breadth of view, clearness, and in an extremely interesting manner. The reader is immediately impressed with the care and thoroughness of the revision, and all of the advances in the science which have been made recently appear in the book. The many important contributions from the laboratory of which the author is Director are embodied, and intimate first-hand knowledge of the subject can be everywhere recognized.

The first part of the book is devoted to general considerations, such as methods of isolation of organisms, sterilization, disinfection; and broad conceptions of the relation of bacteria to disease, immunity, and such subjects are dealt with.

In the second part the bacteria pathogenic to man are individually considered. Here the bacteriology of the diseases due to bacterial infection is discussed, and all recent problems in regard to the relation between specific organisms and disease are taken up in a very satisfactory manner. The modern means of dealing

with various micro-organisms are also given, as well as the principles involved in various sanitary problems.

Special attention has been paid to the protozoa, and the third part of the book is given up to a discussion of these organisms. More emphasis is laid upon the subject than has been the case heretofore in such books, because of the rapidly increasing importance which these organisms are found to have in the cause of certain diseases. The recent work of Wright on actinomyces, of Councilman and his co-workers on smallpox, of Schaudinn and Hoffman on Spirochæta pallida is embodied.

This present edition will surely be of much use as a thoroughly up-to-date and interesting treatise on the subject. G. C. R.

SURGICAL ASPECTS OF DIGESTIVE DISORDERS. By JAMES G. MUMFORD, M.D., Visiting Surgeon to the Massachusetts General Hospital and Instructor in Surgery in the Harvard Medical School, in association with ARTHUR K. STONE, M.D., Physician to Out-patients, Massachusetts General Hospital, and Assistant in the Theory and Practice of Physic in the Harvard Medical School. New York: The Macmillan Co., 1905.

PROBABLY no subject is at present of more interest to the progressive internist and surgeon than that of the surgery of the upper abdomen. Its history extends over but about twenty-five years and is by no means complete. The object of the authors of this volume is to present some idea of what may be accomplished by surgical means in the treatment of diseases of the abdominal digestive organs, and this they have done in an eminently satisfactory manner. Of course, there are a great many questions that are still unanswered; these they have treated very fairly, setting forth the opinions of the various authorities. It must not be supposed that this work is one dealing simply with surgery and especially with the technique of the operations recommended. The book is one that will prove of exceptional value to the general practitioner, to whom it will show the great progress that has been made in the treatment of the diseases of the digestive tract. He will also find it of great aid in diagnosis.

The first portion of the book consists of chapters on the ancient conceptions of the digestive organs and on the methods of diagnosing digestive troubles. This portion is written in an entertaining and comprehensive manner, and is most interesting. The different digestive organs are treated separately, but the authors always keep in view the general relationship between the organ under discussion and its neighbors. A large portion of the book is

given to the discussion of the non-malignant diseases of the stomach, especially ulcer of the stomach and duodenum.

The authors have not burdened their pages with a description of obsolete methods. The operations suggested are well chosen from those practised by the masters in abdominal surgery.

References to literature are frequent and extensive. Illustrations are few, as would be expected in a work of this kind.

The chapter on Abdominal Ptosis, which deals with a subject which is by no means thoroughly understood, is most instructive.

As an appendix there is included a discussion of "Diagnosis in Connection with Surgery of the Stomach," by Henry F. Hewes.

We can heartily recommend this book not only to the general practitioner, for whom it was especially written, but also to the internist and surgeon.

The one objection that we find in the make-up of the book is that it has uneven and uncut pages. The print is exceptionally large and clear. J. H. G.

THE DIAGNOSTICS OF INTERNAL MEDICINE. A CLINICAL TREATISE UPON THE RECOGNIZED PRINCIPLES OF MEDICAL DIAGNOSIS. Prepared for the use of students and practitioners of medicine. By GLENTWORTH REEVE BUTLER, Sc.D., M.D., Chief of the Second Medical Division, Methodist Episcopal Hospital; Attending Physician to the Brooklyn Hospital; Consulting Physician to the Bushwick Central Hospital; Fellow of the New York Academy of Medicine; Member of the Medical Society of the County of Kings, etc. With five colored plates and two hundred and eighty-eight illustrations and charts in the text. Second edition. New York and London: D. Appleton & Co., 1905.

THE second edition of Butler's work has followed hard upon the footsteps of the first, always a sign of popularity. In its present form considerable new matter and illustration will be found. The work consists of two divisions: the first, which comprises about two-thirds of the entire volume, deals with symptoms and indications; the second, with diseases and differential diagnosis. A new chapter has been added on Diseases of the Mind, by W. A. White, and one on the Diagnostic Use of the *x*-ray, by P. M. Pilcher.

The work contains an excellent section on the physical examination of the lungs. The question of blood pressure, a diagnostic aid which is being used with steadily increasing frequency, has been very satisfactorily dealt with. The chapter on the diseases of the nervous system is illustrated with a number of very ad-

mirable diagrams of the motor and sensory pathways. In a work of such wide scope it is hardly possible that some omissions should not have occurred. One regrets that no mention is made of Mackenzie's polygraph for studying the pulse, and that nothing is said regarding the role of the bundle of His in relation to the Stokes-Adams syndrome. No mention has been made of the stereognostic sense, or of sarcomatosis as a cause of superficial lymphatic enlargement, or of carcinoma as a cause of subcutaneous nodules, or of enlargement of the posterior auricular lymph nodes in German measles. Two statements are made to which exception may be readily taken, *i. e.*, that arcus senilis has no special diagnostic value, and that the ordinary method of percussion of the heart "is of little or no use."

We failed to find any mention of Grocco's triangle under pleural effusion, or of cryoscopy, or of the arthralgias, etc., which follow the injection of antitoxic sera. However, the majority of the foregoing omissions are of inconsequential import, and do not seriously militate against the general utility of the book as a work of reference. There is every reason to suppose that the second edition will prove quite as popular as the first. G. W. N.

A Text-book of the Practice of Medicine. By James M. Anders, M.D., Ph.D., LL.D., Professor of Medicine and Clinical Medicine at the Medico-Chirurgical College; Physician to the Medico-Chirurgical Hospital; formerly Physician to the Philadelphia and to the Protestant Episcopal Hospitals, Philadelphia; Fellow of the College of Physicians; Member of the Academy of Natural Sciences, Philadelphia, etc. Seventh edition, thoroughly revised. Philadelphia and London: W. B. Saunders & Co., 1905.

Each succeeding year brings such an increase in the number of medical books offered to the profession that it seems almost as though much of this kind of literature must become a drug on the market. In the general flood it is rather hard to select the more desirable works for our private libraries, but in the case of this volume the fittest seems to have survived, and this fact is attested by the appearance of its seventh edition.

It is a large volume of over 1200 pages and opens, as do most works on Practice, with the consideration of the Infectious Diseases. The reviewer notes that under this head is classified acute articular rheumatism, the chronic articular and muscular varieties being placed in a separate division and classified as belonging

to those diseases which are of probable infectious origin. The latter section includes, besides the above mentioned diseases, such maladies as Weil's disease, milk sickness, foot-and-mouth disease, and glandular fever.

The author rather favors the view that the diplococcus of Coyon and Treboulet is the causative factor in acute articular rheumatism, but does not refer to the investigations of Poynton and Paine.

In the chapter on Syphilis, he refers to the bacillus of Lustgarten, and those isolated by Neissen, Joseph and Piorkowski as possibly responsible for the infection.

Under the head of diseases of the blood and ductless glands, the author in the article on Hodgkin's disease seems to lean to the theory of its non-tuberculous etiology, mentioning, however, the evidence of Musser and Sailer as being opposed to this opinion. In the rather short article on splenic anemia, he does not make use of or refer to the synonym of Banti's disease.

It is noted that in the section on diseases of the pericardium, cardiopuncture is advised in those cases of pericardial effusion in which the nature of the fluid is doubtful.

The use of tables and parallels is systematically adhered to throughout the work, and to the student, especially, these will be useful, particularly in reading the sections on diseases of the nervous system, where they are quite numerous. A. N.

A Laboratory Manual of Human Anatomy. By Lewellys F. Barker, M.B. (Tor.), Professor and Head of the Department of Anatomy in the University of Chicago and Rush Medical College. Assisted by Dean De Witt Lewis, A.B., M.D., and Daniel Graisberry Revell, A.B., M.B., Instructors in Anatomy in the University of Chicago. Philadelphia and London: J. B. Lippincott Co., 1904.

This laboratory manual differs in many respects from similar works and we believe that these differences show improvement. In the first place the nomenclature, which was formulated by the German Society of Anatomists, has been followed. This certainly simplifies the anatomical names for those students who are unfamiliar with Latin and makes the anatomical terms more comprehensive to all. The older terms have been placed in parentheses after the new ones in order to avoid confusion, and at the end of the volume there is an index of the old and the new terms. The author is pleased to see that this nomenclature is being rapidly adopted by many of the best English and American anatomists.

The book is not supposed to take the place of the descriptive text-book or the atlas, but to be a help and guide to the student in his dissection. The author especially tries in the first portion of the book to teach the student in such a way that he may be led into independent thought and work.

The illustrations number 300 and are excellent: the majority of them have been taken from the German atlases. This book will certainly prove the most helpful manual that has been recently published and the student who follows it closely will derive from it the greatest benefit in his anatomical studies. J. H. G.

THE TREATMENT OF FRACTURES, WITH NOTES UPON A FEW COMMON DISLOCATIONS. By CHARLES LOCKE SCUDDER, M.D., Surgeon to the Massachusetts General Hospital. Fifth edition, thoroughly revised, with 739 illustrations. Philadelphia and London: W. B. Saunders & Co., 1905.

IT is unnecessary to say anything in review of this excellent work, as the previous edition was reviewed only about a year ago. We must, however, congratulate the author and the publishers on the marked success which this book has achieved. The present edition is the fifth; it contains some additional illustrations and the text has been modified in certain parts.

As a guide to the treatment of fractures it deserves the high place which it has won for itself. J. H. G.

ATLAS AND TEXT-BOOK OF TOPOGRAPHIC AND APPLIED ANATOMY. By OSKAR SCHULTZE, Professor of Applied Anatomy in Würzburg. Edited, with additions, by GEORGE D. STEWART, M.D., Professor of Anatomy and Clinical Surgery in the University and Bellevue Hospital Medical College, New York. With 25 colored illustrations on 22 Lithographic Plates and 89 Text-cuts, 60 in colors. Philadelphia and London: W. B. Saunders & Co., 1905.

ONE of the greatest helps to the student in studying anatomy is the use of a reliable atlas; in fact, such a work should be considered essential. The present book is a little more than an atlas, as the text, although brief, is concise and complete. It has to deal only with the topographic and applied anatomy, and therefore it will be found of especial value for the practising internist

and surgeon. It is for such that the authors intend the work, and not for the anatomist.

Throughout the volume the relationship between anatomy and the practice of medicine and surgery is never absent from the author's mind. The illustrations are the most beautiful we have ever seen. Most of them are in colors, and these colors are made to represent as nearly as possible the normal coloring of the tissue represented.

We can recommend this book as one of the most satisfactory single volume text-books of applied anatomy. J. H. G.

THE RELATIONS OF DISEASES OF THE SKIN TO INTERNAL DISORDERS. By L. DUNCAN BULKLEY, A.M., M.D., Physician to the New York Skin and Cancer Hospital, etc. Pp. 175. New York: Rebman Co., 1906.

THE pages of this interesting book are dedicated to the many physicians who have from year to year attended the author's clinical lectures on diseases of the skin, covering a period of thirty years. These lectures form the basis of the present volume. So long ago as 1870 a writer in the *British Medical Journal* expressed the opinion that we needed a critical investigation of skin diseases in their relation to diseases of other organs. Are diseases of the kidney or of the liver frequently productive of them? Are diseases of the intestinal or pulmonary mucous membranes frequently associated with those of the skin? These and like questions are taken up seriatim and freely discussed and investigated by Dr. Bulkley, with the result that we have before us an exceedingly valuable contribution, not only to diseases of the skin, but also to general medicine. It is clearly shown as one reads from page to page that the relationship of many cutaneous diseases to disorders of the general economy and to special disorders of organs within the body is often close. Frequently the so-called affections of the skin are the direct result of disorder or disease far removed from the skin in seat. Dr. Bulkley is well known to the profession, no one better as a skilled clinician. He is thoroughly practical, and is at every point endeavoring to show cause and effect. He introduces the reader to the varied subjects touched upon or elaborated in a style that attracts attention and is often convincing. The subjects of digestive disorders related to skin diseases, of hepatic derangements, of urinary disturbances, of nervous disorders, of circulatory derangements, are all taken up and explained as far as possible in the light of experience and the latest investigations. It is on these lines of thought that the author

gives the result of a life-long study based upon an enormous clinical material, backed with abundant, well-digested data, and draws the conclusions that the proper study and interpretation of skin diseases must go hand-in-hand with general medicine. Without this comprehension of the subject, treatment cannot be otherwise than unsatisfactory. It is the fact that skin diseases have for so long a period—centuries, one might almost say—been regarded as distinct from the general ailments of the economy that has heretofore rendered them so obstinate to treatment. All this and much more to the point are ably and clearly set forth in the volume, and we heartily commend the reading of it to all physicians. An hour or so spent with the book will be the means of disclosing the whole subject of dermatology in a new and satisfactory light. The subject-matter is prepared in a systematic manner and is easy to comprehend. A full index adds much to the value of the book.

L. A. D.

ORGANOTHERAPY. By H. BATTY SHAW, M.D. (Lond.), F.R.C.P., Lecturer in Therapeutics, University College, London; Assistant Physician to University College Hospital and to the Hospital for Consumption and Diseases of the Chest, Brompton. Pp. 256. Chicago: W. T. Keener & Co., 1905.

THIS very timely volume, dealing with treatment by means of preparations of various organs, considers the thyroid, parathyroid, and suprarenal glands; substances derived from the alimentary tract, including the pancreas and liver; from the genitourinary organs (testicle, ovary, kidney); from other organs and tissues, as the pituitary body, the thymus, the spleen, hemolymph glands, lymphatic glands, marrow, muscle, nerve tissue, and placenta. It will be found that this work is comprehensive in scope, containing a sufficient number of illustrations, abundantly supplied with references to original investigations, and withal its subject very attractively and concisely presented. As might be supposed, considerably more than one-half of the subject matter is devoted to the thyroid and suprarenal glands; yet if we compare our rapid increase of knowledge along these lines, the results of thorough study of these substances afford us an earnest of what may be expected when the same study shall have been devoted to the other glands, tissues, and substances which are here briefly described, but which are likely to become of almost equal importance. The active practitioner will find within the compass of this little volume what should be of the most urgent interest and a necessity for complete therapeutic information.

R. W. W.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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Uterine Myomas, Heart Disease, and Disorders of the Ovaries.—KESSLER. (*St. Petersburg. Med. Woch.*, 1905, xxx, 421.) The association of degeneration of the heart muscle with myoma of the uterus has in the past few years received a great deal of attention from gynecologists. Striking instances occurring over and over again have directed attention to it. A patient with myoma is admitted to the hospital and dies, without symptoms other than a gradually failing heart, before an operation can be performed. Another patient with myoma after a trivial operation develops marked cardiac insufficiency. Another patient dies suddenly during convalescence from operation after making some slight exertion. In these patients, thromboses and infections frequently and quite unexpectedly occur when there is nothing to account for them but a low resistance, and for this low resistance poor circulatory conditions. Of twenty fatal cases of embolism in gynecological diseases collected by Kessler, 40 per cent. were in patients with myomas. Recently, Fleck has emphasized how very easily these patients are affected by anesthetics. Intoxication symptoms frequently develop before consciousness and the reflexes are lost.

It was assumed that the severe and frequent bleedings, the disturbances of nutrition, and the enforcement of a long-continued rest account for the changes in the heart muscle. But Brasin, in 1893, pointed out that similar conditions existing in carcinoma had no such result. Strassman and Lehmann, in seventy-one carefully recorded consecutive cases, found that 40.8 per cent. showed definite subjective or objective signs of an organic heart lesion. In some of these patients the myo-

mas were very small. Veit, in his text-book, had some years before noted the frequent occurrence of asthmatic attacks in young women with relatively small tumors, and indeed suggested that these attacks were of importance in the early diagnosis of myoma. Veit thought the connection between the two was through the nervous system, but all the evidence is now with Strassman and Lehmann, who refer the dyspnœa to changes in the heart muscle or bloodvessels. These authors go still further and cite instances to show that the cardiac symptoms may develop before there is any suspicion of pelvic trouble. These are points of great importance, as they indicate that instead of being dependent one upon the other both the myomas and the cardiac changes must be referred to a common cause.

The presence of some intoxication to explain both immediately suggests itself, and the ovary has been selected as the possible point of its origin. The influence the ovaries exert upon metabolism is shown in the phenomena of the climacterium, in the diminished oxygen consumption after castration, which can be again increased by feeding oophorin, the increased fat deposit after removal of the ovaries, and the fact that such a serious anomaly as osteomalacia may be brought to a standstill by their removal.

These features are explained as the effects of an internal secretion, and one may assume that under abnormal conditions this altered secretion might be toxic for the heart muscle. This is, of course, all assumption and not capable of direct proof. The remarkable influence the ovaries exert over the circulatory conditions in the uterus is, of course, well known, and as myomas in their development bear such close relationship to the bloodvessels it is possible that changes in the ovaries might lead to their formation. It is of great moment then to note if the ovaries in patients with myomas are always diseased. Fleck states that gross anatomical lesions of the ovaries are always found in patients with myomas, but Kessler believes this to be an over-statement, and is convinced from his own experience and the opinions of others that in many cases the ovaries are at least macroscopically normal. He further offers as objections to the validity of the ovarian hypothesis the circumstance that enucleation of one or more myomas is seldom followed by recurrence, and that myomas may grow very rapidly and attain a large size long after the climacterium.

The clearing up of the points raised in this paper is evidently of the greatest importance in the surgical treatment of these tumors. If the ovaries are at fault the method to pursue is evident. Much valuable assistance must come from the internists who, as a rule, see these cases earlier than the surgeons, and it is particularly in regard to the early stages that statistics are needed. The character of the lesion in the heart muscle also needs to be determined. There is very little carefully collected pathological data.

The Pathogenesis of Tetany.—PINELES (*Deutsches Arch. f. klin. Med.*, 1906, lxxxv, 491) in a previous communication sought to show that tetany following extirpation of the thyroid gland depends upon the destruction of the parathyroids. Clinically, no symptoms of tetany occur if these organs are left. Experimentally, animals with excised parathyroids show symptoms in every manner analogous to tetany in man. Pineles then goes very extensively into all the symp-

toms occurring in the various forms of tetany—the tetany of laborers, the tetany in acute infectious diseases, the tetany in pregnancy, the tetany in stomach disease, and the idiopathic tetany of children—analyzes them all and shows that even in minor details they are analogous to the symptoms observed in tetany strumapriva and to the symptoms of thyroidectomized animals. This remarkable similarity of all the symptoms suggests at once that a single poison is responsible for all. The tetany following the removal of the thyroid in man and animals we know is due to the destruction of the parathyroid bodies. The condition of the parathyroid in the other forms of tetany has not been definitely established.

In connection with this communication it may be well to recall the fact that McCallum in a case of fatal gastric (dilatation) tetany found the parathyroids in a condition of active hyperplasia with numerous mitotic figures, suggesting strongly the possibility that "the parathyroids had become hypertrophied to neutralize large absorption of toxin from the stomach."—*Johns Hopkins Hospital Bulletin*, 1905, xvi, 148.

Endocarditis in Tuberculosis.—Sorgo and Suez (*Wien. klin. Wchnschr.*, 1906, xix, 176) report at length the clinical history of a girl, aged sixteen years, who died of a slowly progressing pulmonary and laryngeal tuberculosis and amyloid disease. The condensed autopsy report reads: Chronic fibroid phthisis with cavity formation of both upper lobes; disseminated miliary and conglomerate tuberculosis in both lower and the right middle lobes; ulcerating tuberculous infiltration of the larynx and trachea; extensive tuberculous ulceration of the ascending colon; scattered tuberculous ulceration in the small intestine; microscopic tuberculous areas in the spleen, liver, and kidneys; amyloid degeneration of the spleen, liver, and kidneys; verrucose endocarditis of the mitral valve.

The endocarditis gave no symptoms during life and was not diagnosed.

Along the border of the aortic segment of the mitral valve and to a much less extent along the border of the opposite segment are numerous pale yellow, uneven, firm, warty excrescences. The largest of these measure about 2 x 4 mm. and are situated just at the free border of the valve. Their central and basal portion consists of compact bundles of spindle-shaped cells, poor in protoplasm which proceed without definite demarkation from the normal valve tissue. The periphery consists of a homogeneous eosin-staining mass indistinctly separated from the dense central portion by a more cellular layer made up of connective tissue cells rich in protoplasm and a small number of leukocytes. In the small nodules the firm connective tissue is often wanting, and they appear to be fastened directly upon the abraded epithelium of the valve. In both forms the interstices are filled with a fibrin net-work enclosing blood corpuscles, principally polymorphonuclear leukocytes, and containing numerous tubercle bacilli. None of the tissue shows any evidence of tubercle formation. Cultures from the vegetations gave a pure growth of tubercle bacilli and no other organisms were found in microscopic preparations.

Cases of true tuberculous endocarditis are rare. From a review of the literature Sorgo and Suez are willing to accept only six reported instances as genuine. The case of Braillon and Tousset is particularly

interesting. Clinically, it ran the course of a septic infection and tubercle bacilli were obtained from the blood during life. At autopsy, tuberculous vegetations were found on the heart valves without pulmonary or glandular tuberculosis, and Braillon and Tousset present the case as one of primary tuberculous endocarditis. It is a matter of difficulty in a given instance to decide whether an endocarditis is tuberculous or not. The histological picture is not sufficient, as under some circumstances tuberculous lesions have no specific structure. The sterility of the vegetations is not decisive, as even septic organisms may disappear from old deposits. Even the presence of tubercle bacilli may be equivocal, as they may have lodged upon an old lesion or have secondarily infected marantic thrombi. The cardiac vegetations not uncommonly found in chronic tuberculosis have been interpreted as tuberculous in nature by one class of authors, and as due to secondary infections by others. Hanot and Londe and Petit have concluded that they are due to the effects of toxins on account of their uniform failure to demonstrate tubercle bacilli.

Michaelis and Blum were the first to approach the problem experimentally. After rupturing the aortic valves through the carotid they injected tubercle bacilli and observed the formation of verrucose vegetations and noted in one case a typical tubercle in one of the vegetations. Of course, these experiments do not represent conditions as they normally occur in patients. Bindo de Vecchi repeated them but was unable to discover in the nodules forming on the valves any specific characteristics. Further, he produced in rabbits corneal tuberculosis and then injected coal-dust into the circulation or else ruptured the valves and in both instances discovered nodules on the valves similar to those obtained by following the procedure of Michaelis and Blum. As the corneal tuberculosis remained strictly localized and as the valve changes present no specific characters he concludes that the deposits are due to the tuberculous toxins. This view was further strengthened by showing that injection of other toxins, namely, diphtheritic, staphylococcic, etc., together with coal-dust produces the same manner of nodules. Prochaskas, working with organisms other than tubercle bacilli found that while various toxins of themselves do not produce endocarditis they do facilitate the lodgement of bacteria upon the heart valves. De Vecchi's experiments need confirmation before they can be generally accepted. Bernard and Salmon by injecting a tubercle bacillus emulsion directly into the carotid or left ventricle observed two kinds of lesions in the valves. The areas were all subendothelial, those between the endothelium and the elastic lamina consisting of a fibrinous exudate with numerous leukocytes and a few scattered tubercle bacilli, but without specific structure, while the areas below the lamina consisted of typical tubercles. These results agree with the observations of Orth, who describes the valvular changes in acute miliary tuberculosis as almost constantly subendothelial, and they illustrate too how definitely tuberculous lesions may lack a typical tubercle formation. Sorgo and Suez think the circulatory conditions in the valve probably explain this difference.

SURGERY.

UNDER THE CHARGE OF

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Spontaneous Cure of Congenital Luxation of the Hip of One Side in Certain Cases of Double Congenital Luxation.—FROELICH (*Revue d'Orthopedie*, January, 1906) says that it not infrequently happens that during the progress of a congenital luxation of one hip the opposite side is found to be equally dislocated. Froelich has found it present when the skiagraphic diagnosis showed the joint to be normal. It is well known that the luxation very often does not exist at birth, but is produced when the child begins to walk, in consequence of defective relations between the femoral head and the articular cavity. These relations may be sufficiently good to permit no defective position of the limb menaced by the luxation. It is when the reduced and evidently affected limb is placed in the abducted position that the displacement occurs on the opposite side, which then seeks an adducted position to preserve the parallelism of the two limbs. Adduction causes the head of the femur on the apparently sound side to rise up over the posterior border of the acetabulum. Not all so-called congenital luxations deserve that name, in the sense that an anatomical predisposition prepares the way for the dislocation. Froelich has seen it occur in the course of subacute arthritis of the hip, due to an attenuated gonococcic infection, or an osteomyelitis.

He reports two cases of congenital luxation in which there was a spontaneous cure on one side. In both, one of the hip-joints is sound as proved by the *x*-rays and examinations. The gait of both is that of a unilateral luxation. One patient was five years, the other seven years old. Skiagrams taken when each was two years old clearly showed double luxations. The parents of one could determine a difference between the original waddling of the child and the unilateral halting which developed later. The presence of a double luxation in an older sister facilitated the comparison. The explanation of the cure is found in the positions assumed by the two limbs during the progress of the cure. In both the luxated side was in adduction. During walking the opposite side must assume the position of abduction to preserve the parallelism of the limbs As already stated, adduction favors the passing of the femoral head over the posterior border of the acetabulum into a dislocated position, while the forced abducted position of the other side favors the gradual entrance of the head into the cavity. In other words nature does what the surgeon does in his efforts to cure a congenital luxation, when he puts the thigh in forced abduction.

The Operation of Mickulicz in Chronic Muscular Torticollis.—Rousseau (*Revue d'Orthopedie*, January, 1906) says that while chronic muscular torticollis is often cured by simple orthopedic treatment or by tenotomy, the more inveterate cases lasting many years and associated with grave scoliosis and extremely marked craniofacial asymmetry require more important surgical treatment to bring about a cure or notable amelioration. He reports such a case in which total extirpation of the muscle, Mikulicz' operation, was performed, with good results. Mikulicz found in his first total extirpations that the spinal accessory nerve was injured, and so he decided to do a partial resection, reserving the more complete operation for a few cases. He made an incision 3 to 4 cm. long, between the sternal and clavicular portions of the muscle. After retracting the edges of the wound he isolated, with his fingers and then divided with a bistoury, the two heads, protecting with a retractor the underlying important structures. Each head was then seized with a forceps and drawn out of the wound. With the finger aided by scissors the muscle was isolated to the junction of the two portions. By exaggerating the pathological position of the head and neck the muscle was gradually drawn further out of the wound and isolated up to the mastoid process. It was there divided, the operator being careful to avoid the external branch of the spinal accessory nerve. Search was then made for any intact fibers which were divided. The wound was closed without drainage, and the head immobilized in the normal position.

The postoperative treatment is very variable, some using plaster-of-Paris, others more or less complicated bandages. In about a week active and passive movements and massage should be begun. The head in most cases finally occupies a normal position, looking forward, but in a certain number it is somewhat displaced as a whole to the sound side, in a few to the affected side. The head and neck are freely movable in nearly all cases. The scoliosis which resulted from the torticollis was with rare exceptions ameliorated, even without consecutive orthopedic treatment.

In all young infants, since the cause of the craniofacial asymmetry is removed, the degree which already exists will almost entirely disappear with time. In patients above fifteen years of age it is but little influenced.

The recurrences which have been reported merely show that very often not only the sternomastoid but all the neighboring parts take part in the process of fibrous degeneration and contraction which is responsible for the deformity, so that every adherent and contracted band must be destroyed. While resection of the muscle may fail in some very rare cases, it is well to bear in mind that it very often succeeds when the other methods have failed.

Rousseau reaches the following conclusions: (1) In very grave, inveterate cases of chronic muscular torticollis the Mikulicz operation should be performed. (2) The total operation is the most efficacious. The spinal accessory nerve on account of its size can easily be dissected. (3) After the operation, orthopedic treatment will be useful to give the muscles of the neck their tonicity and more so especially to correct as far as possible the scoliosis. (4) Sooner or later the situation and mobility of the head will return to the normal, the scoliosis will ordinarily be ameliorated, but usually the craniofacial asymmetry will not be modified.

Sexual Precociousness and Impotence.—FERE (*Annales des Maladies des Organes Genitourinaires*, January 1, 1906) says that precociousness or prematurity is often associated with other anomalies of evolution. It has been shown to be at times a prelude to genius, at other times to insanity, and in some cases a coincidence of a remarkable aptitude with a decided incapacity. It can be followed by a partial imbecility, as impotence, as in a case reported by the writer. To what extent can impotence be relieved by treatment?

By experimentation on the lower animals, especially the rabbit, Fere was successful in some cases in producing an erection with cantharides. It was accompanied by pain, avoidance of the female, and not the least tendency to copulation. Pathological priapism in man does not suggest sexual relations, and toxic priapism can be only sexually imperfect. The cantharides gave a toxic not an aphrodisiac action. The peripheral excitation was not sufficient for copulation.

Phosphorus and strychnine have been extolled for their value in overcoming impotence. Fere has found that they only rarely provoke erection, and then with no desire for sexual relations. The instincts of the lower animals do not call for artificial stimulants. With regard of the use of yohimbine in rabbits, Fere has found that paretic and spasmodic troubles arise from it, but no change in the size or shape of the testicles or penis.

The Diagnostic Value of the X-rays.—DAVIDSON (*British Medical Journal*, January 20, 1906) says that minute particles of metal or glass can be localized in the orbit or eyeball to the one-fiftieth of an inch. The opacity of a substance is in proportion to its atomic weight, so that if the composition of a renal calculus is known then its relative opacity is also known. Uric acid and urate of ammoni acalculi are almost as transparent as flesh; whereas oxalate of lime, phosphate of lime, and even a cystic oxide calculus are fairly opaque, owing to the sulphur in it. It is quite likely that a small uric acid calculus in a stout individual may escape detection.

Primary Suture without Drainage in Acute Appendicitis.—BORELIUS (*Zentralblatt f. Chirurgie*, January 27, 1906) reports one hundred and twenty-three cases of appendicitis from the University clinic at Lund. One hundred and eight were operated on, fifty-nine in the acute stage and forty-nine in the chronic or interval stage. Four died, all in the acute stage. Forty-three were drained. In sixteen the abdomen was closed by layer sutures, the operation being performed from the first to the third day. Healing by first intention occurred in all, except for a superficial stitch abscess in one. The average stay in the hospital was from twelve to seventeen days. Those cases in which drainage was employed remained in the hospital from sixteen to thirty-eight days. In some of these a rubber tube or gauze drain was employed for a few days only, and in them the healing was rapid.

The earlier one operates the more frequently can the abdomen be closed afterward. The decision to close will not depend so much upon the time as upon the condition of the appendix and of the neighboring peritoneum. If the appendix has not perforated and can be taken out without perforation, in general the abdomen can be closed. This may be done also when the appendix is gangrenous if the peritoneal fluid is clear. In eight of the writer's sixteen cases it

was gangrenous, in the other eight only catarrhal changes had occurred. He would counsel the inexperienced operator, if in doubt, to drain freely. The incision may often be small, but should be enlarged according to the needs of the case. The appendix should be removed whenever possible.

Carcinoma of the Breast and its Spread into the Lymphatics.—Lockwood (*British Medical Journal*, January 27, 1906) states that the spread of cancer along the lymphatics depends for its rapidity to a large extent upon the position of the primary growth. In a hollow muscular organ like the urinary or gall-bladder the pause may be months or years. In the mammary gland, which has no capsule, the tongue, or the pharynx, there is hardly any interval of time between the onset of the growth and its spread into the neighboring lymphatics. Lockwood makes an immediate microscopic examination of the smallest and most innocent looking tumors of the breast, and follows this up by a similar investigation of the neighboring glands. Not all enlarged glands associated with neighboring cancer are cancerous. Indeed some of the larger ones may be non-cancerous while the smaller ones are cancerous. In one case of cancer of the breast the axillary glands were shown to be tuberculous. There is little doubt that the lymphatics of the two breasts intercommunicate across the sternum, which explains some of the cases of later involvement of the second breast, although it fails to explain all of them. For instance Lockwood reports one case in which the first breast showed a duct cancer. Within four months a nodule appeared in the opposite breast which was a spheroidal celled carcinoma undergoing colloid change. The subclavian glands demand attention whether the axillary glands are or are not enlarged. Ordinarily, Lockwood contents himself with a thorough dissection above and below the axillary and subclavian veins as far as can be reached by raising the clavicle upward, although when the glands in the neck are evidently involved, he does not hesitate to make an extensive dissection for their removal.

A Case of Polycystic Calculous Nephritis; Anuria; Renal Decapsulation.—Patel (*Annales des Maladies des Organes Genitourinaires*, February 1, 1906) says that on admission to the hospital his patient had not passed urine for six days, and was consequently in a very bad condition. No urine could be obtained by the catheter. She gave a previous history of old attacks of renal colic on the left side, followed by the passage of small calculi. The symptoms seemed localized to the left side and operation was done on that side only. The kidney was studded with multiple cysts, and nephrotomy was considered well-nigh impossible. Instead, as thorough a decapsulation as possible was performed. After operating the urine flowed freely, but the patient died five days later. Autopsy showed both kidneys enlarged and cystic, the right being the larger of the two. In the pelvis of the left kidney were four calculi, in that of the right kidney two calculi. No part of the renal tissue had a normal appearance, but it was hard and lardaceous. The microscope showed that the lesion corresponded more to that of a chronic nephritis with large cysts than to a polycystic kidney.

Renal decapsulation, done in the presence of complete anuria, when nephrotomy is impossible, has re-established the passage of urine. Nevertheless the kidney should be opened, when there is no contra-indication.

THERAPEUTICS.

UNDER THE CHARGE OF

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ASSISTED BY

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The Pneumatic Cabinet in Organic Heart Disease.—Dr. Charles E. Quimby concludes a paper upon this subject with the following statements: (1) The pneumatic cabinet does not cure incurable organic heart lesions. (2) After nearly thirty years' observation and reasonably careful study of results obtained by other methods, in the hands of acknowledged authorities, and fourteen years' personal experience in the use of the cabinet the author is firmly convinced that it affords more immediate, extensive, and lasting relief than any other known measure. (3) That its use is based upon such strictly scientific principles, and the results are so plainly determined by established physical laws, as to justify its description as the nearest approach to the ideal method of treatment in organic cardiac disease.—*Boston Medical and Surgical Journal*, 1906, No. 20, p. 543.

The Treatment of Nervous Pain.—Dr. F. Lots believes that the profession is mistaken in its tendency to neglect these manifestations. The natural tendency to make light of these pains is wrong. The nervous patient is naturally inclined to exaggerate his symptoms, but it is a fact that in many instances his skin is hypersensitive. Consequently, means should be employed to render the cutaneous resistance greater, and this is best accomplished, according to the author, by subjecting the skin to repeated and intense irritation. Frictions with a rough fabric of cotton should be energetically administered and at frequent intervals, the procedure being continued for from one to two hours daily. The pains which respond most rapidly to the treatment are those in the back, those referred to the precordium, and the acroparesthesiæ. In sciatica the frictions are also useful.—*Therapeutische Monatshefte*, 1906, No. 3, p. 118.

The Treatment of Tetanus by Magnesium Sulphate.—Dr. Joseph A. Blake, incited by the fact that magnesium sulphate when injected by lumbar puncture inhibits both afferent and efferent nerve impulses, has employed this drug in the treatment of tetanus; he reports an instance of the disease in which recovery followed five intraspinal injections of 25 and 12.5 per cent. solutions within ten days. The quantity injected of the stronger solution was about 67 minims; of the weaker, which was employed on every occasion except the first, 2 drams. The author reports a second case which resulted fatally, although the magnesium

sulphate injections had a noticeable effect upon the symptoms. He considers that he is justified in claiming that this form of treatment has the following points in its favor: (1) A marked effect in restraining the convulsions and relieving pain, thereby conserving strength and preventing excessive metabolism and heat production. (2) That the spasm of the muscles of mastication is at least lessened, thereby permitting feeding. (3) That the action of the drug is continued for a considerable period (twenty-nine to thirty-seven hours) without depressing action upon the heart muscle. (4) That in one instance at least repeated injections produced no harmful effect, except the inhibition of the bladder and the consequent need for catheterization. No specific action is claimed for the magnesium sulphate, although the drug may have some chemical action upon the toxins. The conservative view is to consider its effect purely symptomatic.—*Surgery, Gynecology, and Obstetrics*, 1906, No. 5, p. 541.

The Treatment of Exophthalmic Goitre.—Dr. Paul Sainton after a considerable experience advises treatment by means of the serum of thyroidectomized sheep. The thyroid gland of the animal is totally excised but the parathyroids are left in place. The first blood is drawn by means of jugular puncture about three or four weeks after the operation; the serum is filtered and rendered absolutely sterile; the addition to it of such antiseptics as carbolic acid does not seem to impair its efficiency. The dosage varies from 35 to 45 minims every two days, depending upon the patient's condition, and the serum is taken in water or wine. The treatment is continued under the same dosage for three or four weeks, when it is discontinued for a week; it is then resumed for fifteen days in every month. The entire duration of the treatment is variable, but usually is from six months to one year, the periods of intermission being lengthened as the patient improves. Under the influence of the serum the size of the thyroid, the exophthalmos, the tachycardia, and the tremors progressively diminish. After the establishment of cure it is best to advise the patient to take the serum for about fifteen days during each following year.—*Revue de Therapeutique*, 1906, No. 7, p. 217.

Jez's Antityphoid Extract in Enteric Fever.—V. Jez reports four additional cases treated by his method and summarizes those hitherto reported by him and others. Of these there have been one hundred, and in all but six, in which the results obtained have been characterized as dubious, the treatment has acted most favorably. There are said to be no contraindications to the administration of the extract and it may be given either hypodermically or by the mouth. The author gives it by the latter channel, and in hourly doses of a tablespoonful. The total amount administered is from 24 to 30 ounces. In the author's opinion and in that of others this is a distinct advance in the treatment of enteric fever, since it causes a rapid amelioration of all the symptoms and shortens the course of the disease from one to two weeks. —*Wiener klinisch-therapeutische Wochenschrift*, 1905, No. 51. p. 1277.

The Calcium Salts in Certain Headaches.—George W. Ross states that there occurs often in women and less frequently in men a headache having the following characteristics: (1) It is present and most severe

on waking and tends to lessen or to disappear in from one to six hours. (2) It is usually a dull, heavy ache or a frontal or temporal throbbing; less often is it vertical, occipital, or unilateral; rarely is it neuralgic. (3) It is chronic and intractable, but may exhibit itself as the common occasional headache to which many are subject. (4) It is associated with a deficient coagulability of the blood. The subjects of this form of headache are usually of the lymphatic type. The expression is heavy and listless, the face is full and the eyes puffy, anemia is often present, and the whole bearing indicates mental and physical lassitude. Symptoms which are often associated with the headache are pain after eating, constipation, œdema of face or extremities, dyspnœa, chilblain or urticaria, and neuralgia. As treatment the author has employed the following in a number of cases with success: A calcium salt has been given in order to increase the coagulability of the blood; the lactate is to be preferred and may be administered in a mixture containing 15 grains of this drug, half a minim of tincture of capsicum, and an ounce of chloroform water, to be taken three times a day before meals. If the lactate cannot be obtained the chloride may be substituted, 15 grains in an ounce of camphor water. Calcium lactate may be combined with bitters and with iron and strychnine, but not with alkalies or alkaline carbonates. The constipation should receive appropriate treatment and the admixture of a certain amount of milk to the diet is advisable. The regimen should be simple; alcohol, shell-fish, and strawberries should be avoided. The author suggests that the calcium salts may be useful in neuralgias when accompanied by diminished coagulability of the blood, and in migraine. He had treated six patients suffering from chronic nephritis with these salts and in five the headaches and œdema were greatly lessened.—*The Lancet* 1906, No. 4299, p. 143.

Drugs in Uric Acid Conditions.—JAMES F. GOODHART believes that all the uric acid solvents, so much vaunted, appear to be equally useless for that purpose, but considers that salines have their value, if given with discrimination, for facilitating the excretory power of the abdominal glands; in this way, water is probably one of the best remedies, but should not be drunk to excess, since the popular belief that water being harmless, and may be drunk in any quantity, is very possibly untrue. In the author's opinion a half-dram of potassium bicarbonate in a glass of water taken at bedtime to stem the nightly tide of uric acid is one of the most useful recommendations, aside from tonics, cures at watering places, and change of scene and air.—*The Practitioner*, 1906, No. 1, p. 9.

The Action of Drugs in Diabetes.—KARL FLEISCHER considers it difficult to decide what action drugs really exert in diabetes, since the elimination of sugar by the urine is subject to spontaneous variations, due to intercurrent conditions, the general state of the patient, and to emotional influences. In his opinion opium produces the most permanent results. Its derivatives are less potent. The theory that diabetes is due to abnormal fermentation has led to the administration of various substances in the hope of preventing these. Most of the drugs given with this idea are of little use, although some of them may prove to a slight extent beneficial.

Aspirin acts well in mild cases and salol may prove effectual. Piperazin given a half-hour after meals, the gastric contents having been previously neutralized by sodium bicarbonate, is appropriate. Many other substances have been given on this theory and upon that that diabetes results from an insufficiency of the glycolytic ferment. Among the latter are beer yeast, hepatic and pancreatic extracts, but these as well as decoctions of various vegetable drugs seem to exert no specific action, with the possible exception of jambul, which, in connection with a proper dietary, may be given to advantage. The author concludes that, with the sole exception of opium, no drug has any specific action in diabetes.—*Therapeutische Monatshefte*, 1905, No. 10, p. 497.

Doyen's Cancer Serum.—ALEXIS THOMSON reports four instances of cancer in which Doyen's serum was administered. The first was a recurrent scirrhus of the breast in obviously hopeless condition from the beginning of the treatment. Injections of the serum were given at intervals, but death took place in about three months; no improvement whatever was noted, but on several occasions there was a temperature reaction. The second was also a recurrent mammary scirrhus in an apparently otherwise healthy woman and fulfilling the conditions laid down by Doyen for successful treatment by means of his serum. A secondary operation preceded by a course of serum injections was decided upon; the operation was performed and followed by further injections, but the growth recurred and, although its progress was slow and the patient's general health was better than is usual under such conditions, death took place seven months after the operation. The third was an unfavorable one for serum treatment from the first. It was an enormous epithelioma of the jaw and treatment was without avail. The fourth was an instance of mistaken diagnosis and not of malignant character. It is interesting solely because the reactions following the serum injections were quite as marked as in the malignant cases described above. The author concludes with the statement that the cases are recorded not because in themselves they afford grounds for deciding the efficacy of Doyen's serum, but because when added to others they may help in the solution of this question.—*The Edinburgh Medical Journal*, 1906, No. 1, p. 53.

Marmorek's Serum in Tuberculosis.—TH. STEPHANY concludes his observations upon this means of combating tuberculosis with the following statements: Marmorek's antituberculous serum has a remarkable curative action in pulmonary, pleural, and osseous tuberculosis. It is able to arrest the course of the disease and to institute cure; under its influence various symptoms, notably pain, are greatly ameliorated. It may be employed without danger, if the technique is proper, in all forms of tuberculosis. The author injects the serum in doses of from 15 minims to 3 drams, depending upon the temperature, reaction, and the local effect, at two-day intervals. He usually employs gradually increasing dosage and intermits the treatment from time to time.—*Le Progrès médicale*, 1905, No. 46, p. 835.

OBSTETRICS.

UNDER THE CHARGE OF

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Palpation of the Ear in Diagnosticating Vertex Presentations.—STOWE (*Surgery, Gynecology, and Obstetrics*, June, 1906) calls attention to the fact that in many complicated and difficult cases it is impossible to reach the fontanelles; especially in forceps delivery, he believes that before the forceps is applied, while the patient is anesthetised, the fingers should be carefully passed over the head to reach an ear. The location of the ear at once gives information concerning the sagittal suture. Further palpation of the ear will enable the obstetrician to determine whether the fingers pass from the occiput to the forehead or from the forehead to the occiput. In this way the physician can recognize the anterior or posterior position of the occiput; the further anterior the occiput is situated the more readily can the ear be felt.

In many cases this method cannot be utilized until the cervix is fully dilated and the patient under deep anesthesia. It does not expose the patient to additional danger.

Lumbar Puncture in Eclampsia.—THIES (*Zentralblatt f. Gynäkologie*, No. 23, 1906) reports seventeen cases of lumbar puncture with extraction of fluid in eclampsia, occurring in Zweifel's clinic at Leipsic. This treatment was carried out not as curing eclampsia, but as diminishing the irritation of the nervous system occasioned by the pressure of cerebrospinal fluid.

The patient was placed upon the side in such a posture that the spinal column was rendered convex and curved backward. The puncture was made 0.5 cm. from the middle line and the needle directed slightly inward. In sixteen of the seventeen cases the spinal canal was entered at once; by this method fluid was allowed to escape very slowly, from ten to twenty minutes being occupied in securing the fluid. When the normal pressure of 120 mm. was secured the needle was withdrawn. During the actual time of puncture there were no symptoms of irritation. In some cases after the puncture there was vomiting, twitching of the muscles, irregularity of the pulse and breathing, and symptoms of irritation of the spinal cord.

The fluid obtained was usually clear, a few leukocytes were present, and in one case the fluid was cloudy, containing abundant leukocytes and a few red blood corpuscles. In one case the fluid was bloody and was thought to indicate hemoglobinemia. After the puncture in this case the convulsions ceased and the patient soon recovered consciousness. During the following night she developed severe jaundice with hemoglobinuria and died in coma. Hemorrhages were found in the liver and in other portions of the body, showing extensive disorganization of the blood.

The tension of the fluid was always raised in eclampsia. When the tension was above 200 mm. the cases were severe and an unfavorable

prognosis was indicated. In one case the tension reached 600 mm. In one case the secretion of urine diminished very considerably after the puncture. The mortality in these cases was high, but the puncture was considered only as a means of lessening irritation and not as a curative measure.

Vaginal Cesarean Section or Retroflexion and Incarceration of the Pregnant Uterus.—BENNECKE (*Zentralblatt f. Gynäkologie,* No. 23, 1906) reports the case of a patient five months pregnant who had retroflexion and incarceration of the uterus. Cystitis was present, with death of the fœtus. As the cervix was long and resisting it seemed safest to empty the uterus by vaginal Cesarean section.

In separating the bladder the bladder wall prolapsed and was ruptured, and urine was discharged. The repture was at once closed by catgut. On examination it was found that the bladder wall had been compressed against the symphysis, producing softening and partial necrosis. The uterus was opened in the anterior wall, the fœtus and its appendages removed, and the uterus tamponed with gauze. The incision was then closed, a permanent catheter being placed in the bladder. Small strips of xeroform gauze were placed anteriorly and posteriorly to the uterus to drain the region of the bladder. The bladder made a good recovery, disturbed for a short time by a brief but not severe attack of cystitis.

Ovarian Pregnancy.—KELLY and MCILROY (*Journal of Obstetrics of the British Empire,* June, 1906) report the case of a multipara in good health, who, after six week's interruption of menstruation was taken with severe pain in both iliac regions. This was followed by intermittent vaginal hemorrhage. The patient lost strength and weight and was admitted to the hospital. On examination there was tenderness over the left iliac region, but no tumor could be detected. The uterus was slightly enlarged; the left appendages formed a considerable mass, tender to pressure; while the right appendages were also exceedingly tender. After some delay abdominal section was performed, and on the left ovary was found a bloody cyst as large as a good-sized plum. The ovary and tube were removed. The patient made an uninterrupted recovery. On examination of the specimen the tube was found involved. The pregnancy had been ovarian and chorionic villi and syncytium were detected. The whole ovisac was composed of ovarian tissue. The pregnancy had been within a Graafian follicle. Lutein cell tissue was found almost directly adjoining fœtal tissue, separated from it by a layer of fibrin and connective tissue. No rupture had occurred, but at the lower portion the tissue was greatly thinned out. No decidual cells were found in the Fallopian tube. The fœtal structures were entirely surrounded by ovarian tissue.

Ectopic Pregnancy.—HAULTAIN (*Journal of Obstetrics of the British Empire,* June, 1906) reports his experiences in thirty cases, supposed to be ectopic pregnancy. Some of these were wrongly diagnosticated, so that the number verified by operation was reduced to twenty-three. The most common symptoms were pelvic discomfort and irregular bleeding. The least constant symptom, in fact a very rare symptom, was expulsion of decidua. The bleeding which occurs in these cases

is probably a conservative process on the part of nature to prevent rupture of the thin Fallopian tube. The reason why the expulsion of the decidua is so rare is found in the fact that the decidua is not expelled until after the death of the ovum. The symptoms of pain, and sometimes shock, are caused by the escape of blood into the abdomen, usually through the abdominal end of the Fallopian tube; this occurs before the rupture. In these cases there is not sufficient blood to produce a considerable tumor; as the process is very gradual, severe shock often does not develop. The predominant symptoms are those of pain and irritation. When rupture of the tube occurs the predominant symptom is shock. Attention is called to the difficulties of diagnosis, and cases are narrated in which ovarian cysts with ruptured vein and pedicle, ovarian abscess and salpingitis, bicornate uterus, and intestine distended with feces have all simulated ectopic pregnancy. Uterine abortion is frequently diagnosticated when ectopic gestation is present. Operative treatment alone is satisfactory, and the writer ligates both ends of the sac of the embryo and then enucleates the sac from the broad ligament, stitching together the tissues with a fine continuous suture. In old cases in which blood has been enclosed between the layers of the broad ligament, the cavity is packed with sterile gauze, the end of which is pushed through an opening into the vagina. Four deaths occurred in this series of cases, from purulent peritonitis, severe hemorrhage, secondary rupture, and exhaustion. All the fatal cases were operated upon late.

Extrauterine Pregnancy, with Uterine Fibromyoma.—TAYLOR (*Journal of Obstetrics of the British Empire*, June, 1906) reports a case of extrauterine pregnancy admitted to the hospital in severe shock from prolonged hemorrhage. The uterus was symmetrically enlarged, and it was thought that extrauterine and intrauterine pregnancy were present. The patient died and upon examination of the uterus it was found to be the site of a fibroma. Taylor reviews the literature of the subject, adding a bibliography.

GYNECOLOGY.

UNDER THE CHARGE OF

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Resistance of Tissues to Cancer.—MAASS (*Newyorker med. Wochenschrift*, Band xv, No. 3) has been led to believe from personal observation that the tissues of certain individuals resist the spread of cancer even when there is extensive cell-infiltration. The disease long remains localized, metastases either do not occur at all, or develop more slowly than the original neoplasm. That cancerous foci may long remain localized until they finally overcome the resistance of the surrounding tissues, or until younger and more active epithelial cells develop, is shown in the case of late recurrence after operation.

This individual idiosyncrasy may be utilized practically after operation by treating the cancerous foci which remain with caustics that are not sufficiently powerful to destroy the zone of healthy protective tissue. The writer believes that the good results sometimes observed by the injection of erysipelas toxin are due not so much to their specific action as to the fact that by the mild grade of inflammation which they induce increased tissue-resistance is favored.

This resistance may be augmented by systematic nourishment of the patient, proper environment, etc.

Best Method of Curing Cancer of the Uterus.—PFARMENSTIEL (*Berliner klin. Wochenschrift*, No. 27, 1905) believes that the ultimate solution of this question lies not so much in the removal of the intrapelvic lymph nodes as in the thorough extirpation of outlying foci of disease in the tissues adjacent to the neoplasm. If the broad ligaments are once involved a radical operation is only possible by the abdominal route, even though the immediate mortality must always be relatively great. This applies especially to cancer of the cervical canal, the best prognosis being in younger subjects, during pregnancy, or soon after the puerperium. Incipient epithelioma of the portio may be treated by vaginal hysterectomy, with extensive resection of the vagina and parametrium. The clinical character of the growth should determine to some extent the choice of operation, the vaginal route being applicable to cancer of the hard, ulcerating variety, while in the cauliflower form abdominal hysterectomy is indicated.

If after opening the abdomen the glands are found to be extensively diseased it is better to abandon the operation at once.

Relation of Uterine Disease to the Development of Cancer.—POLESE (*Rassegna o'ost. e gin.; Zentralblatt f. Gynäkologie*, No. 9, 1906) believes that prolonged irritation of the cervix uteri is an important etiological factor in the production of cancer. In thirty-four out of forty-eight cases this was clearly shown. The writer divides these cases into three classes: (1) Stenosis and dysmenorrhœa. (2) Chronic uterine catarrh. (3) Laceration of the cervix. In a number of cases microscopic examination showed a "sclerotic" condition of the uterine mucosa. The writer advises early "prophylactic" operation in every suspicious case.

Treatment of Pruritus Vulvæ.—LEREDDE (*Rev. prat. des mal. cutan., syphil., et vener; Zentralblatt f. Gynäkologie*, No. 9, 1906) recommends highly the use of zinc paste, which he applies to the inner and the outer surfaces of the labia majora and minora, previously tamponing the vagina, the tampon being renewed after each urination. This treatment is not to be employed if actual lesions of the skin are present. Radiotherapy is a valuable adjunct in this connection.

Sarcoma of the Uterus.—PIQUAND (*Revue de Gyn. et de Chir. abdominale*, Band ix, No. 3) from an analysis of 416 cases collected from the literature concludes that the etiology of sarcoma of the uterus is practically unknown, neither Cohnheim's theory, heredity, trauma, inflammation, previous sterility, etc., being demonstrable etiological factors. As regards the age of the patient, he found that sarcoma may develop

at puberty as well as after the climacteric. Contrary to cancer, the favorite site of sarcoma is in the body of the uterus, the latter being affected in 325 out of 393 cases in which the location of the neoplasm was stated. Metastases are most common in the lungs, next in the liver and intestines, the bloodvessels (rarely the lymph-vessels) being the channels of infection.

Changes of the Ovaries in Vesicular Mole.—WALLART (*Zeitschrift f. Geb. u. Gyn.*, Band lvi, Heft 3) from studies of the ovaries in connection with vesicular mole and chorion epithelioma arrives at the conclusion that in these conditions, as well as in normal pregnancy, the cells of these interna often undergo an epithelioid transformation, with accompanying cystic degeneration of the follicles, but that there is no accompanying change peculiar to the malignant condition of the uterus.

The Dangers of Atmokausis and Zestokausis.—PINCUS (*Zentralblatt f. Gynäkologie*, No. 13, 1906) affirms that if the operation is properly performed there is no more reason why it should be followed by stenosis, atresia, or obliteration of the uterine cavity than should a simple curettement.

He repeats the cautions so often given that an exact diagnosis must first be made and that the uterine cavity must be entirely empty, even of mucus and blood-clots. Atmokausis should not follow curettement in women who are still in the childbearing period. Malignant disease must always be excluded. The writer still adheres to his origina belief that total extirpation of the uterus should never be performed for hemorrhage alone until atmokausis has been tried.

Bloodvessels of the Uterus.—Keiffer (*Zentralblatt f. Gynäkologie*, No. 18, 1906) from careful anatomical studies arrives at the following conclusions: The branches which are given off from the uterine artery pursue a spiral course through the parenchyma of the uterus, each having a connective-tissue covering derived from that of the uterus. The arterioles gradually lose their three layers until the smallest are in direct contact with the uterine muscle and connective tissue. The latter form a dense net-work, the terminal vessels not presenting a visible lumen unless they are injected. In the gravid and inflamed uterus the net-work of vessels present the appearance of ampullæ.

The veins have contractile coats and are in direct contact with the parenchyma. Keiffer concludes that the uterus is a true erectile organ, subject to marked increase in size under the influence of nervous and vasomotor influences.

Defect of Bladder and Urethra.—MACKENRODT (*Zentralblatt f. Gynäkologie*, No. 21, 1906) reports the case of a young girl with hypospadias of the urethra and neck of the bladder, who had submitted to several unsuccessful operations. The reporter cured the patient by adopting a different plan from the previous operators, suturing the neck of the bladder directly instead of utilizing flaps from the bladder, it being his observation that in such cases a rudimentary sphincter vesicæ can nearly always be found.

In a second case the urethra and neck of the bladder sloughed away

in consequence of some lesions attending a difficult delivery. In this case also he was able to dissect out from a mass of cicatricial tissues the ends of the vesical sphincter and to unite them, afterward making a new urethra by a plastic operation, the result being entirely satisfactory. He lays stress upon the fact that however perfect may be the anatomical result after repair of the neck of the bladder by a plastic operation the innervation will be faulty unless the natural sphincter is restored.

Degeneration of Uterine Fibroids.—WINTER (*Zeitschrift f. Geb. u. Gyn.*, Band lvii) believes that sarcomatous degeneration occurs in 4 per cent. of all cases of fibromyoma and in 9 per cent. of the submucous variety. Seventeen cases of necrosis occurred under his own observation, hence this must be regarded as a comparatively common form of degeneration, which should be suspected, especially when persistent hemorrhages, contractive pains, and symptoms of autoinfection follow abortion or labor at term.

Cystic degeneration the writer believes to be due to defective nourishment of the neoplasm, especially after the menopause, and is indicated clinically by profuse hemorrhages, with local and general disturbances.

Paralysis after Gynecological Operations.—GLOCKNER (*Zentralblatt f. Gynäkologie*, No. 21, 1906) reported at a meeting of the Leipzig Obstetrical Society the case of a patient, aged thirty-two years, who in the eighteenth day after normal convalescence from hysterectomy developed paresis of the lower limbs without loss of sensation. Since hysteria and a central lesion could be excluded the diagnosis of neuritis was made, although the reporter was unable to explain its origin or to find any records of a similar case.

Prof. Windscheid, to whom the patient had been referred for diagnosis and treatment, while he had no doubt that the case was one of neuritis, was equally unable to present a satisfactory explanation. He suggested as possible etiological factors the position of the patient during operation, injury to nerves, or anemia or toxemia.

Castration in Cancer of the Breast.—ROUBAND (Thèse de Lyon; Abstract in *Zentralblatt f. Gynäkologie*, No. 22, 1906) has collected fifty-one cases of inoperable cancer of the breast in which both ovaries were removed. In twenty-three the neoplasm either disappeared completely or diminished in size, but in only three was the cure permanent. In twenty-eight the result was entirely negative.

Helmitol in Postoperative Cystitis.—WITTHAUER (*Zentralblatt f. Gynäkologie*, No. 23, 1906) in view of the good results obtained in the treatment of cystitis (especally the postoperative type) with helmitol was led to administer it as a prophylactic whenever the use of the catheter was necessary. Fifteen grains are given twice daily, but the bladder is also irrigated with boric acid solution after each catheterization. 26 cases are reported in which the patient was catheterized from three to twelve days after operation, in only one of which did cystitis develop (A weak point in this report is the fact that irrigating the bladder was employed in addition to the use of helmitol.—H. C. C.)

OPHTHALMOLOGY.

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PROFFSSOR OF DISEASES OF THE EYE IN THE PHILADELPHIA POLYCLINIC.

The Knife-needle Operation for Secondary Capsular Cataract.—JACKSON (*Arch. of Ophthal.*, March and May, 1906) emphasizes the difficulties and dangers of operating through the clear cornea, as ordinarily recommended, and suggests the proper position of the point of entrance and technique of the operation, of which the following is the summary: The knife-needle should always enter through the vascular tissue of the limbus. It should be absolutely sharp, and used so as to cut and not tear. The operation should be done under strong illumination. The incisions must be made completely joining each other at or in the angle. Attention to these points will render the operation with the single knife-needle effective in almost all cases of secondary capsular cataract, and make it one of the safest operations of surgery.

Extraction of Cataract in the Capsule.—HENRY SMITH (*Arch. of Ophthal.*, 1905, No, 6) describes his operation of extraction in the capsule. He makes a liberal-sized upper incision, inserting the knife at the sclerocorneal junction, and cuts into the cornea half-way between a normal pupil and the sclerocorneal junction. The speculum is then removed, and an assistant hooks up the upper lid on an ordinary large-sized strabismus hook and draws down the lower lid by placing the ball of his thumb on the skin of the face close to the eyelid. This is kept up until the operation is finished. It is of supreme importance to inhibit the action of the orbicularis by such pressure. He then places the curve of a strabismus hook over the cornea, about the junction of the lower with the middle third of the lens and a spoon, just above the upper lip of the wound. He presses the strabismus hook down, neither toward the wound nor from it, and does not alter its position until the lens is nearly out, all the time making slow, steady, and uninterrupted pressure and counterpressure. When the lens is more than half-way out, while keeping up the tension with the spoon in its original position, he shifts the strabismus hook forward and gently tilts the lens by getting the edge of it in the concavity of the strabismus hook. This must be done with great care and without the slightest roughness or jerk, to prevent the rupture of the capsule and the escape of the lens. An antiseptic pad and bandage are applied. After the lens and its capsule have come out there is to be no "fiddling," otherwise the vitreous is sure to escape. A table of 2616 cases of extraction in the capsule performed in the hospital from May, 1904, to May, 1905, shows first-class results in 99.27 per cent., second-class results in 0.38 per cent., and failures in 0.34 per cent. The first-class results include: Iritis,

0.3 per cent.; escape of the vitreous, 6.8 per cent.; capsule bursting, 8 per cent.; capsule left behind, 4.28 per cent. No written description can teach the operation satisfactorily; it requires to be seen. Pagenstecher has also extracted the lens in its capsule, but the procedure is entirely different from the Indian operation. In the former the lens is lifted out on a spoon.

The Treatment of After-cataract.—SMITH (*Arch. of Ophthal.*, March and May, 1906) strongly urges that the best operation for cataract and the procedure of the near future is extraction within the capsule; when this has not been done but the cataract has been extracted in the ordinary manner, leaving the capsule behind, he recommends removing the membrane in whole or in part by making an iridectomy sized wound at the sclerocorneal junction above; doing an iridectomy, if it has not already been done; introducing an ordinary iris forceps, a little stouter than usual, somewhat beyond the centre of the pupil; allowing the blades to open wide; driving the point through the after-cataract wide apart; close the forceps tightly, and bringing out the offending body. Thus treated the capsule usually comes out in its entirety; and if not in its entirety, it comes out more efficiently than by any needling. There may be an escape of a bead of vitreous, which is of no importance. The escape of vitreous should not occur if an assistant keeps the lower lid well drawn down by placing his thumb on the face below it. In this procedure the object of removing the offending body is commonly accomplished, and the results are eminently satisfactory.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES.

UNDER THE CHARGE OF
J. SOLIS-COHEN, M.D.,
OF PHILADELPHIA.

Fibrosarcoma of the Thyrohyoid Membrane.—RENSHAW (*Journal of Laryngology, Rhinology, and Otology*, April, 1906) reports a case of fibrosarcoma arising from the thyrohyoid membrane. In a weaver, twenty-nine years of age, a growth had steadily developed, during a course of two years, over the thyrohyoid space and upper part of the thyroid cartilage. The voice had been hoarse for ten months and there had been some difficulty in swallowing, while lately there had been considerable pain running up to the left ear.

A smooth swelling in the middle line extended from immediately below the hyoid to about half-way down the thyroid cartilage, spreading on each side almost to the posterior margin, and appeared to be tightly bound down to the thyroid cartilage. It was firm and elastic to the touch, but there was no tenderness upon pressure.

Laryngoscopic inspection showed the laryngeal mucous membrane to be congested, the entire anterior wall to be displaced slightly back-

ward, while there was also a slight bulging observed in the middle line and a little above the anterior commissure.

The tumor was removed by a median incision and was found to be definitely encapsuled under the thyrohyoid muscle. The patient made an uninterrupted recovery with relief of his symptom. Renshaw attributed these symptoms to pressure of the growth under the cervical fascia forcing the larynx backward.

Congenital Lipoma of the Buccal Pouch.—WYLIE (*Journal of Laryngology, Rhinology, and Otology*, January, 1906) recently removed from a female patient, aged fifty, a congenital lipoma of the buccal pouch which had formed a firm, smooth projection into the mouth, and had caused but slight inconvenience. The structure was adipose tissue with an ill-defined fibrous capsule. It represented an hypertrophied vestige of the "infant's sucking pad."

Multiple Telangiectasis of the Skin and of the Mucous Membranes of the Nose and of the Mouth.—KELLY (*Revue hebdomadaire de Laryngologie, d'Otologie, et de Rhinologie*, April 28, 1906) reports two instances in sisters, and refers to eight other cases that he has found in literature which he has studied in connection. These cases usually terminate fatally by hemorrhage or by exhaustion due to the hemorrhages.

Multiple Angiomas of the Throat.—DE NAVRATIL (*Archives Internationales de Laryngologie, d'Otologie, et de Rhinologie*, Mai-Juin, 1906) alludes to a patient he saw in Dr. Dollinger's clinic with angiomas upon the left tonsil, palatine folds, and the conjunctiva, associated with a large erectile tumor upon the left side of the neck. During narcosis for extirpation of the neoplasm, asphyxia supervened, which was attributed by the operator to the angiomas in the palate and throat which became hyperemic during the arterial hypertension, and dilated sufficiently to obstruct the respiratory passages. Tracheotomy was immediately performed and the operation then completed. Three days later the cannula was removed, and the patient left the clinic soon after.

Œdema of the Pharynx.—SCHADLE (*The Laryngoscope*, February, 1906) reports a case in which unilateral œdema of the pharynx occurred in sequence from an infectious nephritis brought on by an attack of quinsy of the same side.

Soft Fibroma in the Lateral Wall of the Pharynx.—JOHN MCCOY (*The Laryngoscope*, February, 1906) reports a cystic looking growth as large as a small pear which had hung free by a small pedicle in the cavity of the pharynx of a man, thirty-seven years of age. The only symptoms complained of had been that of a lump in the throat for some six months.

Hypertrophic Laryngeal Tuberculosis.—RHODES (*The Laryngoscope*, January, 1906) reports a case of hypertrophic laryngeal tuberculosis in a man, thirty-six years of age, the subject of tuberculous disease in the knee-joint. The diagnosis was confirmed by the detection of giant cells and numerous tubercle bacilli in a section of the right ventricular band removed for purposes of microscopic study.

DERMATOLOGY.

UNDER THE CHARGE OF

LOUIS A. DUHRING, M.D.,
PROFESSOR OF DERMATOLOGY IN THE UNIVERSITY OF PENNSYLVANIA,
AND
MILTON B. HARTZELL, M.D.
INSTRUCTOR IN DERMATOLOGY IN THE UNIVERSITY OF PENNSYLVANIA.

A Fatal Case of Erythema Multiforme Exudativum.—WELANDER (*Archiv f. Dermatologie und Syphilis*, Band lxxvii, Heft 2) under the above caption reports the following case: A young man, aged twenty-three years, who had multiple initial lesions of syphilis upon the penis, was ordered daily inunctions of mercurial ointment, and a hypodermic injection of mercurial oil every five days. At the end of two weeks a conjunctivitis appeared with an erythematous eruption situated upon the backs of the hands and upon the knees, accompanied by mild fever, chills, and malaise. After some days these symptoms began to disappear, but soon a new attack with severe fever and extensive eruption, with swelling and redness of the mucous membrane of the mouth, appeared. The buccal mucous membrane became excoriated, was covered with a grayish-yellow exudate, and was very painful. The fever increased in severity without any new skin symptoms, a nephritis and symptoms referrable to the respiratory organs appeared, and the patient finally died with symptoms of general infection. [It seems to us the possibility of this case being one of mercurial poisoning is not excluded.—M. B. H.]

Experiments upon the Action of Light in Hydroa Estivalis.—EHRMANN (*Archiv f. Dermatologie und Syphilis*, Band lxxvii, Heft 2), from a number of experiments made with the Finsen apparatus upon a man the subject of hydroa estivalis, draws the following conclusions:

The summer eruption of Hutchinson or the hydroa estivalis of Bazin is due to a familial, probably hereditary, idiosyncrasy of the skin against the action of the actinic rays of light, and is analogous to epidermolysis bullosa congenita hereditaria, in which there is a hypersensitiveness against mechanical irritation; with this difference, however, that in the latter a diminution of the idiosyncrasy occurs with advancing years and tolerance does not occur as in summer eruption. As being more appropriate, Ehrmann proposes to call the affection epidermolysis or dermatolysis photactinica congenita.

Ringworm with Unusual Localization.—RILLE (*Dermatologische Zeitschrift*, Band xii, Heft 11) at the seventy-seventh meeting of the Deutsch Naturforscher und Aerzte presented a patient with ringworm in a most unusual situation. A man, forty years old, had had for twenty years a diffuse reddening, scaling, and infiltration of the forearms, backs of the hands, and palms, an abundance of fungus elements being demonstrable in the deeper layers of the epidermis. There were also a characteristic ringworm of the finger-nails, a trichophytic blepharitis, and reddening and scaling of the external ear. The skin about the angles

of the mouth was red and scaling, the adjoining mucous membrane and red of the lips were bluish white and thickened. On the borders of the hard and soft palate were irregularly circumscribed macules and epithelial defects, with bluish-white opacities. On the back of the tongue, in the median line, especially the posterior half, were numerous pinhead to hemp-seed-sized, yellowish-red and dark-red, solid-feeling nodules, some of which showed shallow ulcers. A moderate amount of the trichophyton fungus was demonstrable in the lesions in the mouth. The affection of the mouth had lasted about eight years.

Static Electricity in the Treatment of Diseases of the Skin.—SUCHIE (*Dermatologische Zeitschrift*, Band xii) reports a number of cases of chronic eczema, sarcoma, epithelioma, and some parasitic dermatoses in which he has had most successful results from the use of static electricity. Of special interest is the report of a case of mycosis fungoides of three years' duration, which after the failure of all other methods of treatment was apparently completely cured by this agent. The author regards static electricity as of extraordinary value in the treatment of many diseases of the skin, but it is necessary to use strong currents. Undesirable effects are never observed after its employment, even when the current is allowed to act for long periods of time.

A Peculiar Case of Circumscribed Seborrhœa.—MARSCHALKO (*Dermatologische Zeitschrift*, Band xii, Heft 11) reports a peculiar case of profuse circumscribed secretion of sebum occurring in a woman, aged thirty-three years. About eleven months before coming under the author's observation she had received a severe blow with a club in the supraorbital region, which resulted in a purulent inflammation and was followed by anesthesia in the left supraorbital region. Some time afterward she began to suffer from increasingly severe neuralgic pains, for which she underwent a surgical operation, in which some fragments of bone were removed. The pain continued, however, and gradually a profuse greasy secretion made its appearance upon the injured side. When first seen the patient presented a most peculiar appearance; the left frontal and temporal regions were covered by a sharply circumscribed, dirty brownish-yellow, thick mass the surface of which was divided into polygonal areas as in ichthyosis sebacea. The patient experienced severe pain from the slightest touch, and it was with the greatest difficulty that a portion of the mass, which was slightly adherent, was removed. The skin beneath the crust was somewhat hyperemic, and from the dilated follicles minute drops of half-fluid white fat projected. The secretion was confined to a region corresponding very exactly to the distribution of the supraorbital nerve. In this region there was decided hyperalgesia with hyperthermalgesia. Treatment directed against the abnormal fat-secretion was without result. A second operation was performed on account of the increasing severity of the neuralgia; this was followed by a diminution of the pain and secretion of fat.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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Pathological Histology of Congenital Syphilis in Relation to the Spirocheta Pallida.—LEVADITI (*Ann. de l'Inst. Pasteur*, 1906, t. xx, p. 41) has been able to demonstrate Spirocheta pallida, often in great numbers, in the organs of six fœtuses from syphilitic mothers. By staining in bulk with silver nitrate small bits of the tissues hardened in formalin the organism may be seen in sections, and their distribution studied. They were found in decreasing numbers in the liver, lung, suprarenal glands, and skin, but always predominated in any organ which showed pathological change. In the lungs of a child who died of pneumonia alba they were very numerous. The parasites seemed to have a marked preference for the epithelial cells in which they seemed to lie. Besides, they invaded the vessel walls. They also seemed to undergo phagocytosis, for frequently the parasites were found in the large macrophages. The author belives that for this reason they are not common in the spleen. The maceration of the fœtus *in utero* is thought to depend upon some autolytic action which is set up after death from an intense infection by Spirocheta pallida.

Immunization against Swine Plague by the Help of Bacterial Extracts (Aggressins).—BAIL and others have shown that exudates produced in the body by the injections of certain bacteria have the property of enhancing the virulence of these same bacteria when injected with them into other animals, though if injected alone they are harmless. Wassermann and Citron have been able to obtain identical substances, so-called aggressins, from aqueous extracts of bacteria. Citron (*Zeit. f. Hyg. und Infekt.*, 1906, Band lii, p. 238) by injecting guinea-pigs and rabbits with 2 to 4 c.c. of these aggressin substances poured from exudates produced by the bacillus of swine plague or from serous or aqueous extracts of the bacillus itself has been able to immunize the animals against many times the fatal dose of a culture of swine plague. He finds, moreover, that the serum of immunized rabbits has a very definite quantitative protective power for guinea-pigs and mice against injections of fatal doses of swine plague.

Toxin of Fatigue.—WOLF-EISNER (*Centr. f. Bakt.*, 1906, Bd. xl, p. 634). Weichardt in 1904 advanced the theory that manifestations of fatigue were produced by a toxin generated in the overexerted organism which is similar to diphtheria, ricin, abrin, and tetanus toxins. For this fatigue toxin an antitoxin could be produced which *in vitro* and *in vivo* would neutralize it.

Wolf-Eisner in discussing this question puts forth the idea that athletic training may produce an immunity to this toxin, and thus allow the trained athlete to perform much more work than the untrained.

A fatigue toxin was obtained from animals fatigued by mechanical and experimental means which when inoculated into other animals in small doses produced symptoms of fatigue: drowsiness and a lessening of activity. The toxin is easily absorbed from mucous surfaces, and so it was administered in the experiments by spreading it on the conjunctiva. Death often follows the administration. A genuine antitoxic immunity was produced by the non-fatal doses.

The fatigue toxin was not found in the blood of animals, but in the muscles, while the blood contained the antitoxin. The toxin is not dialysable, while the antitoxin can be dialysed with ease. This difference the author thinks accounts for the fact that the antitoxin is found in the blood while the toxin is not.

The fatigue toxins have the properties of colloidal, high-molecular, albuminous bodies. The author thinks, however, that this may be due to the fact that the toxins cannot be separated from the albuminous bodies and so appear to be very similar to them.

It has been found that the use of the antitoxin of one animal is harmless to an animal of another species. The author believes that certain conditions, such as are found in neurasthenia, may be due to the lack of antitoxin production. By the breaking down of albumins by electrolysis, toxins can be formed which can also produce an antitoxin. The fatigue toxin is probably of this nature.

The Toxicological Constitution of Amanita Phalloides.—W. W. FORD (*Jour. of Exp. Med.*, 1906, vol. viii, p. 437) has shown in earlier papers that extracts of the poisonous mushroom Amanita phalloides contains a hemolytic principle, phallin, previously described by Kobert in 1891, which acts directly upon red blood corpuscles without the intermediation of serum, and is destroyed only at a temperature of 65° or higher. The hemolytic principle according to the author should be placed provisionally with the bacterial hemolysins. The extracts themselves are deadly poison to animals which, however, may be immunized against fatal doses. The immune serum is antihemolytic in a high degree.

This paper deals with the separation of a second substance from the hemolytic factor. Certain of the effects produced upon animals, such as hemoglobinuria and pigmentation of the spleen, could be accounted for by the action of phallin, but it was discovered that if the phallin was removed by treating the extract with red blood corpuscles the extract was still highly toxic. Heating to 65° destroys the hemolytic action without injury to the toxic factor. Extracts treated with emulsions of brain tissue remain unaffected. Finally, animals immunized with a hemolytic-free extract produce a serum which is not antihemolytic but antitoxic.

The author concludes that the extracts of the poisonous mushroom contain at least two substances: phallin, a thermolabile substance, which is the hemolytic principle, and in animals produces the subcutaneous œdema, hemoglobinuria, and pigmentation of the spleen; and a second body, termed by him amanito-toxin, which is thermostable, and in animals gives rise to hemorrhage, necrosis, and fatty degeneration of the organs.

The Path of Infection or Tubercle Bacilli from the Mouth and Trachea to the Lung, with Special Reference to the Condition in Children.—BEITZKE (*Virch. Arch.*, 1906, Bd. clxxxiv, p. 1) to determine the relationship between the various systems of lymphatic channels in the neck and bronchial regions has injected the lymphatics, starting at various situations, in cadavers of newborn children. By this means he has determined that fluid injected into the chain of great, deep, cervical lymph glands does not reach the thoracic vessel. There are no communicating branches between the two systems. It is also impossible to inject through the recurrent chain of superficial lymph glands the deep glands. The separation lies at the level of the lower edge of the thyroid gland. On the other hand, injections through the group of cervical lymph glands lateral to the sternocleidomastoid muscle flow into that part of the deep cervical chain lying underneath, though the reverse is not true. The latter chain ends in a gland directly above the omohyoid, and occasionally in a gland beneath this muscle. This gland may be injected through the tracheobronchial lymph glands partly direct, partly by means of the recurrent chain of glands. Either anteriorly or posteriorly to the vena anonyma sinistra the lymphatics of both sides anastomose. Further experiments carried out upon dogs in which India ink was rubbed upon the tonsils, etc., showed that there was only one method of transmission of these particles from the cervical lymphatics to the lung—namely, through the blood stream. A study of the lymphatic tuberculosis in forty-five tuberculous children who came to autopsy demonstrated that this method, though practical, is not necessary. Infection of the lungs and of the bronchial lymph glands is much more common by aspiration of tubercle bacilli into the bronchial tree. An ascending cervical tuberculosis frequently occurs independently. The aspirated bacilli may be held in the air; they may also be acquired through the mouth when they are taken with infected food.

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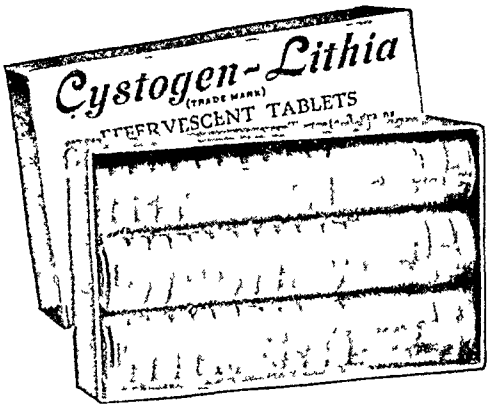

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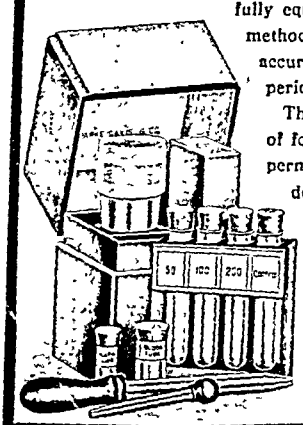

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